CASE STUDY
The Mysterious Case of Patient X: A Case Study for Neuroscience Students

Judith Mosinger Ogilvie
Department of Biology, Saint Louis University, St. Louis, MO 63103.

The Mysterious Case of Patient X is adapted from an actual clinical case of a famous American writer whose symptoms initially presented as Parkinson's disease. His complex medical history challenges students to investigate alternative diagnoses. Students confront the complexity of biomedical systems from the molecular and cellular processes that underlie neuronal degeneration to the organization and integration of brain regions that control the symptoms of disease.

The case is written for upper-level undergraduate or beginning graduate students in biology or neuroscience but could be adapted for introductory neuroscience courses.

Key words: case study; project-based learning; collaborative learning; Parkinson's Disease; parkinsonism; dopamine; neuroanatomy

BACKGROUND AND CONTEXT
The American Association for the Advancement of Science report, Vision and Change In Undergraduate Biology Education: A Call to Action (Brewer & Smith, 2011), provides a foundation of core competencies that all students in biological sciences, including neuroscience, should develop through their undergraduate education. These include the ability to apply the process of science, i.e., constructing new knowledge by formulating hypotheses and testing a hypothesis with observations and data. Also included are development of effective communication skills, within and beyond the discipline, and the ability to relate key concepts to society. Case studies provide an excellent tool for building these skills and have been demonstrated to increase student engagement, motivation and self-confidence (White et al., 2009; Yadav et al., 2007).

A case study tells a story. The Mysterious Case of Patient X is the real-world story of one of America's greatest storytellers. Eugene O'Neill is the only American-born playwright to be awarded the Nobel prize in Literature ("All Nobel Prizes in Literature," 2019) in addition to four Pulitzer Prizes for Drama. His most famous play, "Long Day's Journey into Night," is a semi-autobiographical drama that addresses addiction, alcoholism and the impact of these disorders on family dynamics. O'Neill died in 1953 at the age of 65 after suffering for more than a decade with a degenerative neurological disorder diagnosed as Parkinson's Disease (PD), although the symptoms and progression were atypical. His widow requested an autopsy in order to get a more complete and accurate diagnosis. The results, however, were sealed at her request. Decades later, the surviving grandchildren agreed to the release of the autopsy results. This case study is adapted from the publication of those results in the New England Journal of Medicine (Price & Richardson, 2000).

Parkinson's Disease is a member of a larger family of parkinsonian syndromes, sometimes called atypical parkinsonian disorders or simply parkinsonism (Brooks, 2002; Williams & Litvan, 2013). For this case study, the term Parkinson's-like disorder (PLD) is used because it less well defined, fostering greater exploration by the students. PD is generally characterized by four key symptoms: tremors, rigidity, bradykinesia, and a shuffling gait. PLDs share many of the motor symptoms associated with PD. However PD is generally distinguished by an asymmetric onset that continues as the disease progresses and, importantly, by a responsiveness to treatment with dopaminergic agonists (Lew, 2007). The latter is a direct consequence of the underlying pathology that characterizes PD: loss of dopaminergic neurons in the substantia nigra and the presence of protein aggregates called Lewy bodies. Today, many PLDs have been characterized and researchers are actively seeking diagnostic tools and therapeutic approaches to these disorders. Although much less was known about the wide range of PLDs in the mid-20th century, differential diagnosis continues to be a significant challenge. This case study challenges students to confront the complexity of biomedical systems ranging from the molecular and cellular processes that underlie neuronal degeneration to the organization of the brain regions that control the symptoms of disease.

The Mysterious Case of Patient X was developed for an upper-level undergraduate course on Neurobiology of Disease. The pathology report includes family history as well as behavioral, neurological, systems and cellular analysis, providing a broad foundation that can be adapted for many different courses. The original publication has been modified here using the interrupted case method with two scenes and an epilogue. Student materials and implementation notes are available from the corresponding author or from cases.at.june@gmail.com.

LEARNING OBJECTIVES
Content Objectives
At the end of the unit, students will be able to:
- describe the progression of PD symptoms and how these relate to brain regions affected by the disease
- describe the criteria for diagnosis of PD
- explain the biological mechanism underlying treatment
options for PD including side effects of DA agonists
• list known causes and risk factors for PD and explain
  the difference
• compare and contrast PD to other related disorders
• apply knowledge of PD to explain why Patient X’s
diagnosis is not PD
• describe the significance of the substantia nigra and
  the anatomical progression of PD pathology
• define α-synuclein and Lewy bodies and explain how
  they contribute to PD pathology
• describe the proteolytic pathways that are implicated in
  α-synuclein processing.

Process Objectives
At the end of the unit, students will be able to:
• develop and justify a hypothesis based on available
  diagnostic criteria
• critically evaluate reliability and accuracy of biomedical
  information from internet resources
• clearly articulate neuroscientific questions and
  concepts in a group setting
• demonstrate collaborative problem-solving skills.

CLASSROOM MANAGEMENT OVERVIEW
This case is comprised of two scenes and an epilogue. The unit is taught in four 75-minute class periods but could
be easily adapted to less class time. Students should have
a basic understanding of neuroscience. Some knowledge
of brain structure is helpful, but not required.

1. Prior to beginning the case study, students learn the
symptoms, criteria for diagnosis, treatments, causes
and risk factors associated with PD. This could be
included in lecture material prior to beginning the case
study. An alternative problem-based learning approach
is presented here, in which students consider what they
already know, what they don’t know, and then to work in
small groups to find the information supported by
reliable references. Students research PLDs as a
homework assignment.

2. The Mysterious Case of Patient X: Part 1 – The Patient
presents the patient’s demographic and family history,
general medical history, and the neurological
progression of the disease. Students consider what
information supports the diagnosis of PD and what
alternative PLDs should be considered.

3. The Mysterious Case of Patient X: Part 2 – Postmortem
Findings presents the autopsy results, detailing the
anatomical structures of the brain. Again, students
consider what information supports the diagnosis of PD
and to identify alternative PLDs.

4. The Mysterious Case of Patient X: Part 3 – Epilogue
concludes the case study presenting the analysis and
final conclusions of the pathologists that performed the
autopsy. Biographical information about Eugene O’Neill
is also provided. The name of the patient is not
revealed until the end in order to prevent students from
finding the diagnosis through an internet search.

This case study provides a launching point for more
advanced discussion of misfolded proteins and protein
aggregation. Several genes that are mutated in familial PD
are known to function in autophagy and ubiquitin-
proteasome pathways. This topic provides a common
thread for a wide range of neurological disorders
characterized by protein aggregation, including PD,
Alzheimer’s disease, Huntington’s disease, Amyotrophic
Lateral Sclerosis, and prion diseases (Ciechanover &
Kwon, 2015).

CASE EVALUATION
Direct Assessment
The Mysterious Case of Patient X has been taught four
semesters. Direct measures of student learning were
assessed through classroom participation, assignments
and exams. Homework assignments were checked at the
beginning of class but not collected until the end, in order
to facilitate class participation. Students notes added to
the assignment during class were to be clearly indicated.

The exam format was adjusted each year to
accommodate modifications in the overall structure of the
course. In Spring 2017, the Parkinson’s unit was assessed
with a take-home exam that asked students to develop a
hypothesis and design an experiment emphasizing
material covered beyond the case study. Sample data
from the three semesters that were assessed with an in-
class exam is shown in Table 1. These exams served as
the primary means of assessing learning outcomes. They
included multiple choice, short answer, and, in some
cases, an essay question. Students consistently did very
well on multiple choice questions. Not surprisingly,
students did better in small classes with less than 10
students than in the larger class with 28 students.
However, in all cases, students performed well above the
proficient level, defined as 80%.

Student self-assessment was performed through both a
structured survey and an open-ended three-minute
reflection. Prior to this unit, the course used two major
case studies making it impossible in most cases to
determine the relative contribution of The Mysterious Case
of Patient X to their responses. The prior cases relied on a
problem-based learning approach exemplified by Professor
Eric Can’t See: A Project-Based Learning Case For
Neurobiology Students (Ogilvie & Ribbens, 2016).
Nevertheless, some student responses were specific to
this case and, since it was taught at the end of the
semester, it was likely to bias their responses.

Indirect Assessment
In 2019, students were given both a pre- and post-
assessment survey (Fig 1). At the beginning of the
semester, students rated their level of experience critically
evaluating information in the popular press or internet
about neurobiological disorders. On a scale of 1 (no
experience) to 5 (extensive experience), the average self-
assessment was 3.1 ± 0.98. On the post-assessment
survey, students rated how much learning they gained for
this element on a scale of 1 (no gain) to 5 (very large gain).
Table 1. Examples of learning objectives assessed on the unit exam are shown with types of questions and student performance. 2015, n = 9; 2018, n = 7; 2019, n = 28.

<table>
<thead>
<tr>
<th>Learning Objective</th>
<th>Type of question</th>
<th>Average Grade 2015</th>
<th>Average Grade 2018</th>
<th>Average Grade 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Describe the criteria for diagnosis of PD.</td>
<td>Short answer</td>
<td>98.6%</td>
<td>96.4%</td>
<td>92.5%</td>
</tr>
<tr>
<td>Explain the biological mechanism underlying treatment options for PD including side effects of DA agonists.</td>
<td>Short answer</td>
<td>100%</td>
<td>97.6%</td>
<td>85.7%</td>
</tr>
<tr>
<td>Compare and contrast PD to other related disorders.</td>
<td>Short answer</td>
<td>NA</td>
<td>NA</td>
<td>98.2%</td>
</tr>
<tr>
<td>Apply knowledge of PD to explain why Patient X’s diagnosis is not PD.</td>
<td>Short answer</td>
<td>91.7%</td>
<td>96.4%</td>
<td>87.7%</td>
</tr>
<tr>
<td>Define α-synuclein and Lewy bodies and explain how they contribute to PD pathology.</td>
<td>Multiple choice</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

The average score was 4.2 ± 0.88, with 100% of the students indicating some level of gain and 78% indicating large or very large gain. In the pre-assessment survey, students rated their level of experience actively participating in class discussion with an average score of 3.8 ± 0.81. In spite of this strong response, students indicated that they had moderate to large gain (3.5 ± 1.13) with 29% of the students indicating very large gain. Using the Likert scale (1 = strongly disagree; 5 = strongly agree), students also rated their level of agreement with the statement: I gained knowledge by learning from my classmates and/or by explaining to them. Notably, 89% of students agreed or strongly agreed with this statement (4.33 ± 0.78).

Finally, students were given the following question for a three-minute reflection: “What is the most interesting knowledge you have gained in this class? Why?” Box 1 includes sample responses. Many students commented here and in the university course evaluation that they expected to hate the collaborative learning approach in the class and were surprised to discover how much they loved it, consistent with their responses on the post-assessment survey. Students found The Mysterious Case of Patient X to be “challenging and engaging.” Students also appreciated that this was a real case of a well-known individual. Overall, the self-report data support student fulfillment of the process objectives.

SUMMARY AND FUTURE DIRECTIONS

The Mysterious Case of Patient X is presented as the third and last major case study of the semester. Self-reported data from reflection papers and post-assessment surveys

<table>
<thead>
<tr>
<th>Box 1: Sample student comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;I really enjoyed the case study about [Patient X].... It was challenging and engaging.&quot;</td>
</tr>
<tr>
<td>&quot;It was so interesting learning about the actual physiological/anatomical issues that are the potential or actual cause of diseases.&quot;</td>
</tr>
<tr>
<td>&quot;The most interesting thing I learned from this class was how certain diseases are so similar in biological mechanisms. I also learned how to critically look at scientific [information].&quot;</td>
</tr>
<tr>
<td>&quot;Discussing case studies as a class was interesting as sometimes other students will point out new ideas or observations.&quot;</td>
</tr>
<tr>
<td>&quot;The most interesting part of this class was the approach. I've never been in a collaborative learning course before. I thought I would hate it, but I loved it.&quot;</td>
</tr>
<tr>
<td>&quot;Most interesting → how to collaborate to self-learn topics.&quot;</td>
</tr>
<tr>
<td>&quot;I think the most interesting thing I have gained from this class is not necessarily knowledge, but the process in which to think about the brain in a new way.&quot;</td>
</tr>
</tbody>
</table>

Figure 2. Sample student comments.
indicate that the approach is successful in student attainment of both content and process learning objectives. This is supported by student performance on exams demonstrating that content objectives were successfully met.

This case study can be adapted in several ways. It can be shortened by introducing basic information on Parkinson’s disease in a lecture format rather than having students research this information in small groups. Assignments may be done individually as homework rather than as groups in class. Having the instructor present more of the background information, would enable the case study to be adapted for introductory level neuroscience courses, where students can appreciate the complexity of the nervous system at the gross level, without necessarily delving into the molecular and cellular systems, that may be more appropriate for an advanced course. Future plans are to add discussion of primary literature that focuses on the biological mechanisms underlying Parkinson’s disease. The Journal Case Study format (Prud’homme-Généreux, 2016) provides an excellent tool for this addition.

REFERENCES


Received Month, July 31, 2019; accepted September 4, 2019.

The author thanks Ken Long for the initial concept, Elena Bray-Speth for valuable discussion on pedagogical approaches and members of the Neuroscience Case Network for their helpful comments and feedback. The Neuroscience Case Network is supported by an NSF RCN-UBE grant #1624104.

Address correspondence to: Dr. Judith M. Ogilvie, Department of Biology, Saint Louis University, 3507 Laclede Ave., St. Louis, MO 63103. Email: ogilviej@slu.edu

Copyright © 2019 Faculty for Undergraduate Neuroscience

www.funjournal.org