# ARTICLE Mystery Neurotransmitters! An Active Learning Activity on Synaptic Function for Undergraduate Students

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A core learning objective of undergraduate neuroscience education is an understanding of synaptic function and neurotransmission. This article presents a critical thinking activity in which students explore and evaluate neurotransmitter function at the synapse. Students analyze fictional datasets to identify fundamental processes involved in synaptic function, first following evoked neurotransmitter release and then in response to two "mystery" drugs. The activity requires students to synthesize information from multiple datasets in order to interpret data and figures, skills crucial to science literacy. Students' self-reported

Essential learning objectives in an undergraduate neuroscience program include a mastery of basic neuroscience knowledge and an ability to think critically and integratively (Kerchner et al., 2012). A fundamental component of basic neuroscience knowledge is synaptic function and neurotransmission. In a survey of undergraduate neuroscience faculty, over 75% of respondents reported that an understanding of the cellular and molecular functions of neurons, including neuronal communication, is essential to undergraduate neuroscience instruction (Kerchner et al., 2012). Synaptic function and neurotransmission are typically covered early in introductory neuroscience courses, as they lay the groundwork for subsequent physiological and systems-level units (e.g., Kalat, 2013). However, these topics are often reviewed and/or revisited in upper-division neuroscience courses (e.g., psychopharmacology) and are also covered in many introductory and advanced psychology and biology courses.

Pedagogical approaches that incorporate opportunities for active learning and critical thinking have been shown to promote higher-order cognitive skills (Bloom, 1956; Hake, 1998; Armbruster, 2009) and positively impact student attitudes (Armbruster, 2009), exam scores (Armbruster, 2009; Freeman et al., 2014), long-term retention (Halpern & Hakel, 2003), and translatable skills (Bonwell & Eison, A growing number of problem-based learning 1991). activities and case studies have been developed for use in neuroscience classrooms (e.g., Meil, 2007; Roesch and Frenzel, 2016; Cammack, 2017). However, a search of the online database Educational Resources in Neuroscience (ERiN; http://erin.sfn.org/; Olivo et al., 2015) identified few classroom-friendly activities specific to synaptic function (Table 1). While many engaging laboratory-based activities and demonstrations on synaptic function are available via ERiN and other sources (e.g., Xu-Friedman, 2013; Wyttenbach et al., 2014; Lemons, 2016), courses that lack perceptions and declarative knowledge following the activity suggest that this activity promoted critical thinking and deep learning related to synaptic function. The activity is amenable to collaborative, team-based learning and can be modified for a range of undergraduate courses in neuroscience, psychology and biology.

Key words: synapse function; neurotransmission; drug abuse; pharmacology; neuroscience; undergraduate; active learning; classroom activity

laboratory sections or have limited instructional resources must rely on critical thinking activities amenable to nonlaboratory classroom settings.

The present paper presents a classroom-based activity on synaptic function. The activity, "Mystery Neurotransmitters," requires that students apply their understanding of basic principles of synaptic communication to analyze figures depicting fabricated datasets. After completing this activity, students should be able to (a) describe three ways in which a neurotransmitter's action in the synapse might be terminated (i.e., reuptake, degradation, diffusion), (b) compare/contrast expected levels of neurotransmitter in the synaptic cleft terminal ("extracellular") and in presynaptic the ("intracellular") over time, using each of these mechanisms, (c) evaluate how different types of drugs might affect one or more of these mechanisms, (d) predict the abuse liability of these drugs, based on their ability to disrupt normal synaptic function and their time course of action, and (e) synthesize information from different sets of figures to understand a typical set of scientific results. The activity is based, in large part, around analyzing and interpreting data and figures, which is considered to be a major goal of undergraduate neuroscience education (Kerchner et al., 2012) and is crucial to science literacy.

This activity was used in an introductory neuroscience class comprised of psychology and biology majors but it is flexible enough to be used, in full or in part, in science courses of different sizes, levels, and disciplines.

# THE *"MYSTERY NEUROTRANSMITTERS"* ACTIVITY

Students were assigned to read Chapter 2 (Synapses) of the course textbook (Kalat, 2013) during the third week of the course. Nerve cells, action potentials, and neuroanatomy were covered during prior weeks of the course. Previous in-

# of educational	search term				
resources	synapse	synaptic	neurotransmission	neurotransmitter	
lab exercise	0	4	0	1	
assignment	4	11	1	1	
case study	0	0	0	0	
discussion group	0	0	0	0	
simulation	1	3	0	1	

Table 1. Results from a search of the ERIN database on 6/24/16.

class lectures on neurotransmitters covered the first four steps of neurotransmission (synthesis, packaging, release and action at target sites). These lectures focused on small molecule neurotransmitters (e.g., glutamate) and included diagrams on the whiteboard. Each stage of neurotransmission was added onto these diagrams and numbered (1-4), with the fourth being target sites for neurotransmitter action (e.g., ionotropic and metabotropic receptors on the pre- and post-synaptic membranes). To introduce the fifth step (clearance), the *"Mystery* Neurotransmitters" activity was completed during a single class session, on the final day of the neurotransmission unit.

The activity begins with a brief explanation on why rapid termination of a chemical signal (i.e., neurotransmitter) can be useful for meaningful communication between neurons, then summarizes the major mechanisms by which neurotransmitter action is terminated in the synapse (i.e., reuptake into the presynaptic terminal via membrane-bound transporters, enzymatic degradation in the synapse, or simple diffusion). The activity is then divided into two fictional scenarios. Major goals of the two parts of the activity are to (a) introduce the idea that endogenous neurotransmitters allow chemical communication between neurons (Part 1), and (b) emphasize the variety of ways by which exogenous drugs can alter normal chemical communication (Part 2).

In Part 1, a team of neuroscientists has discovered two neurotransmitters, each released by a different neuron and Students whose identities are unknown. must compare/contrast the concentrations of each neurotransmitter and its primary metabolite in the presynaptic terminal and in the synapse in order to identify the potential mechanism(s) by which that neurotransmitter is removed from the synapse. For instance, falling extracellular levels and rising intracellular levels of the neurotransmitter suggest that the neurotransmitter is being transported back to the presynaptic terminal. Rising extracellular transmitter and/or metabolite levels suggest that enzymatic degradation is occurring. Students are also asked to compare the data from both neurotransmitters to determine which of them is cleared from the synapse more rapidly, and to predict how the data might look different following exposure to a drug that blocked reuptake.

In Part 2, the team helps law enforcement officers to identify how two new street drugs impact dopaminergic neurotransmission at the synapse. A brief description of the mesolimbic dopamine system is provided, and select references are included for more nuanced descriptions of this complex topic (e.g., Salamone & Correa, 2012; Berridge, 2012; Salamone et al., 2018). Students must compare/contrast dopamine levels in the presynaptic terminal and synapse to determine (a) how dopamine is typically cleared from the synapse and (b) how each drug affects normal dopaminergic signaling. These drugs are based loosely on classic psychostimulants (cocaine and amphetamine).

Extending the ideas from Part 1, students must now determine how each drug changes dopamine's storage, release, and/or clearance from the synapse, requiring them to integrate additional information about synaptic function (storage/release) with their working understanding of clearance mechanisms in order to interpret the graphical data. This aspect of the activity requires that students have already learned the first four stages of neurotransmission, via assigned readings and/or mini-lectures as described earlier in this section. Students are also asked to predict metabolite levels in the presence of each drug, add those data to the appropriate figure, and describe the factors that they considered in formulating their answer. Finally, students evaluate which novel drug seems potentially more dangerous by considering factors such as the scale and persistence of the drug-induced changes.

A major aspect of this activity is data and graphical literacy. Students must read and interpret figures and their legends, compare/contrast information on multiple graphs, and add expected data to a graph. Throughout this activity, students must integrate information from both the intra- and extracellular graphs in order to find the best answer. Such tasks require higher-order cognitive skills of analysis, synthesis, and evaluation (Bloom, 1956), and are consistent with a growing emphasis on undergraduates' ability to describe and interpret data as a hallmark of scientific literacy (Association of American Medical Colleges-Howard Hughes Medical Institute, 2009; American Association of American Medical Colleges, 2010; Kerchner et al., 2012).

To complete this activity, students joined 2-3 nearby peers to answer questions as a small group. Teams were given approximately 15 minutes to complete each of the two parts of the activity. After each part, groups volunteered to share their thinking/answers with the class and I reviewed the rationale behind answers that were consistent (or inconsistent) with the data presented in the figures. At the end of the activity, I drew connections between the mechanisms of action of the two novel street drugs from the activity and actual drugs that have similar mechanisms of action (e.g., cocaine as a reuptake inhibitor). The class period ended by introducing the idea that drugs can cause persistent changes to synaptic function that can contribute to tolerance and dependence; these ideas could be expanded upon in a separate lecture.

This activity was not scored and was instead used to engage students in problem-solving and creative thinking and to spark discussion about the fifth stage of synaptic transmission (clearance). If needed, the instructor could easily develop a scoring system for this activity.

It is worth noting that the time course of the actual mechanisms of reuptake, degradation, and diffusion are affected by many factors, such as transporter density, and are still a matter of some debate (M. Xu-Friedman, personal communication). The figures in this activity are intended to reflect general mechanisms of neurotransmitter clearance (e.g., movement from the synapse back into the presynaptic terminal) and may not be reflective of the actual time course of these (still unclear) mechanisms within individual neurons. Instructors of more advanced courses might use this issue as a teaching moment and discuss mechanistic and technical factors contributing to this fabricated dataset.

The activity utilizes a fictitious technology (i.e., probes that measure intra- and extracellular concentrations of a small-molecule neurotransmitter), which allowed me to meet my primary pedagogical goals while approximating (though certainly not replicating) existing neuroscientific techniques. The data are based loosely on the time course of voltammetry samples (e.g., Gerhardt et al., 1984; Garris et al., 1994; Champagne et al., 2004). Specific details about techniques and analytical tools used to measure neurotransmitter levels, such as voltammetry (e.g., Fortin et al., 2015; Garris et al., 1994; Wu et al., 2001) and microdialysis (e.g., Justice, 1993; Young, 2004), were omitted from this activity for simplicity and length considerations. However, comparison of such techniques would be an interesting topic for a supplementary minilecture associated with this activity, depending on the instructor's expertise, course goals, and interest in discussina various neuroscientific techniques of neurotransmitter levels or even neuronal activity (e.g., calcium imaging, in vivo electrophysiological recordings).

#### STUDENT RESPONSES TO THE ACTIVITY Methods

Participants were undergraduate students, aged 18-22, enrolled in a 200-level introductory neuroscience course at a small liberal arts university in Tennessee. The course prerequisite was completion of an introductory 100-level psychology course. The course was comprised of sophomores, juniors, and seniors. Most (84%) students were psychology majors and 20% were neuroscience minors. To participate in the study, students needed to have participated in the "*Mystery Neurotransmitters*" activity (see Supplementary Material). No other inclusion/exclusion criteria were used. The Institutional Review Board of The University of the South approved the study prior to its initiation.

Study participants were recruited orally at the end of the class period in which "*Mystery Neurotransmitters*" was completed. A written announcement containing a link to the study materials, hosted by Qualtrics (www.qualtrics.com), was posted to the course Blackboard site after class, and anyone with the link could access the Qualtrics survey anonymously. The Qualtrics link contained the informed consent form, which described the study as exploring "how students responded to the recent in-class activity on synapse function." Students were told that I was interested "in their opinions" about the study and that they would complete a brief questionnaire and short ungraded quiz, both of which would be anonymous and have no bearing on their coursework. Students had to consent to participate in order to begin the study.

The instructions on the first page of the survey read, "I am interested in how you responded to our recent in-class activity on synapse function ("Mystery Neurotransmitters"). Please read each question carefully, and answer each question <u>honestly</u>. In order for me to assess what parts of the activity made the most impact, please put away your activity and do not refer to it as you answer the following questions." The students were reminded that their answers were anonymous and could not be linked to their name.

The questionnaire included Likert-type and open response questions. The Likert-type questions are listed in Figures 1-2. The scale ranged from 1 (strongly disagree) to 9 (strongly agree), with 4 being neutral. N/A was also an option but was not selected on any question. Open-response questions provided a source of qualitative data. Some questions were negatively worded (e.g., "I did not understand the purpose of this activity") and reverse-coded during analysis and for presentation purposes (Figures 1-2), in an effort to prevent positive response biases and use of response sets (e.g., answering all "9"s without reading each question carefully).

The quiz consisted of true-false and open response questions. Questions are listed in Table 2. Open response questions were graded out of two points, mimicking how a similar exam question might be graded (0-incorrect; 1-partial credit; 2-full credit).

On the informed consent form, participants were told that they would complete an ungraded guiz but not that the guiz would include declarative knowledge outcomes. After completing the study, participants were shown a debriefing form that stated that I was also interested in the information that they retained from the activity and my rationale for withholding that information (e.g., preventing them from looking up answers). Participation was voluntary and data remained anonymous. Demographic information (e.g., gender, major) was not collected to enhance participant privacy. Participants who opted to receive compensation received a small gift card to a local coffee shop; while this is standard for study participation, it could have biased assessment results. A departmental colleague handled compensation to protect participants' identities. Students could participate for two weeks after the Qualtrics link was distributed.

#### Results

Sixty-four percent of the class (n=16) participated in the study. Over a third of the students (37.5%) participated on the first day that the Qualtrics link was available; all but two students participated within a week. Had a larger sample size been available, it would have been interesting to assess decay of knowledge over time. The relatively small sample size is a limitation to this study, but does offer initial evidence that this activity was well received.

Students' self-reported perceptions and interest in the "*Mystery Neurotransmitters*" activity were positive and favorable (Figures 1-2). For transparency, all questionnaire questions are presented in Figures 1-2, with the exception of one question that was omitted from analysis (see below). Students' overall rating of this activity, on a scale of 1 (low) to 10 (high) was a mean of

This exercise helped me to understand the basic principles of synapse function

I feel comfortable explaining 1-2 ways in which NT action can be terminated

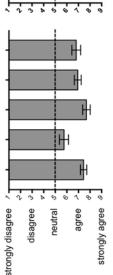
This exercise helped me understand different ways in which drugs of abuse might act on synapses

> The process of identifying different [synaptic] mechanisms helped me realize that not all neurons function in the same way

This exercise helped me to think creatively about how NTs might act at the synapse

I feel comfortable evaluating NT levels in a synapse using graphs/figures1

It was helpful to compare/contrast figures showing NT levels in response to different fictional drugs



I was motivated by the premise of finding out more about fictional street drugs

This activity increased my interest in studying how different NTs act on synapses

> This activity increased my interest in studying how drugs act on the brain

This activity increased my interest in studying animal behavior

I enjoyed this activity

Figure 1. Students' self-reported perceptions and interest in the activity. Data are presented as mean +/- SEM. <sup>1</sup> denotes questions that were negatively worded and reverse-coded for analysis and presentation. "NT" was used to abbreviate "neurotransmitters" here but not in the original questionnaire.

8.50 and standard deviation of 1.03; a one-sample t-test showed that these ratings differed significantly from 5.5, the neutral rating (t=11.619, df=15, p<0.001). The median score was 8.5. Throughout the activity, students asked thoughtful questions that demonstrated their efforts to understand the graphs and their meaning. Students' responses to the question, "What did you enjoy most about this activity?" that addressed the activity's content included:

"An opportunity to think creatively."

"This activity took the basics of what we had learned in class and took them to the next level of thinking which helped increase my understanding of the topics."

"Having to spot the dynamic interactions between the different mechanisms acting on neurotransmitters."

"It allowed me to further understand the differences in which drugs can affect the mechanisms of the brain in such drastically different ways."

"I enjoyed learning how drugs can affect the ... synaptic cleft.'

"The comparison of the two different street drugs on dopamine."

"I enjoyed being able to connect the fictional drugs we studied to real world drugs or abuse to understand more about the effects of drugs on our brains."

Students also responded positively to the structure and presentation of the activity as a small-group exercise (Figure 2). Related students' responses to the question "What did you enjoy most about this activity?" included:

"the graphs made it so much easier than just seeing the figure on the board and trying to visualize how it worked."

"it was interactive and not just a lecture. l also enjoyed working in a small group to come up with the answers."

"there were frequent pauses to explain the answers."

"...working in a group and getting everyone's opinion on the question to solve the problem."

"...the opportunity to explain and discuss confusing parts of the exercise with other members of the class."

"...working in a small group and then discussing our answers with the class as a whole."

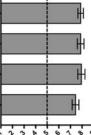
Students' responses to the question "If you were going to summarize this activity in 1-2 take-home points, what would they be?" indicated that they met key learning objectives:

"There are three different ways to get rid of neurotransmitters: reuptake, enzymatic breakdown, diffusion."

"Neurotransmitters interact with cells in various ways and the effects can be manipulated by various drugs."

"Neurotransmitters' storage, release, and removal can be influenced in a variety ways depending on the drug that is consumed."

"Neurotransmitters and chemicals in the brain are always in flux and that with that knowledge be able to better combat and prevent certain drugs from working."



"The rate of the release and disposal of neurotransmitters affects how the body responds"

"Every neurotransmitter affects the brain in a different way and these ways can be altered through the use of legal/illegal drugs"

One question from the questionnaire ("This activity provided the answers for me") was intended to assess students' perceived self-efficacy as they worked to come up with answers with their teammates. However, we also reviewed the answers together in class, so this question could have been interpreted in multiple ways and was thus omitted from analyses.

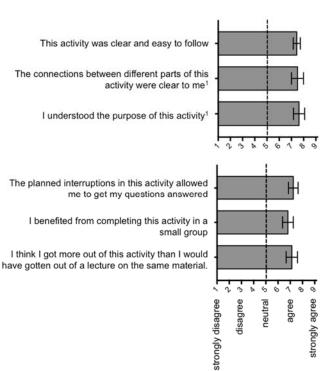
Participants also performed well on declarative knowledge questions. Most participants (56%) got all true/false questions correct and performed well on the short-answer questions (Table 2). Many students provided reasonable answers to the second short-answer question ("...two potential factors...") but these factors were not specific to the *"Mystery Neurotransmitters"* activity and instead referred to prior course content that, while technically correct, was not the intent of this question. Question 5 ("...all synapses contain...") is worded in a slightly ambiguous way and may have required a more nuanced answer than a true/false question could capture, which may explain why fewer students answered correctly, but was included here for transparency.

A caveat to the data presented in Figures 1 and 2 is that they are not specific to the activity itself. Students' responses to these questions may have also been influenced by course activities surrounding this assignment (e.g., assigned Kalat reading or mini-lecture preceding the activity) and/or by the dynamics of the small team of classmates with whom they completed the activity (e.g., being on a team with a particularly strong student).

Since these assessments were collected, the activity has been adjusted slightly for clarity, based on reviewer feedback. The updated *"Mystery Neurotransmitters"* activity is available as supplementary material to this article; the key is available by request to the author.

#### DISCUSSION

This activity was implemented during a unit on synaptic communication and neurotransmission in an introductory neuroscience course. Prior to starting the activity, students completed an assigned reading on synapses (Chapter 2, Kalat, 2013) and heard a mini-lecture by the course instructor on the stages of synaptic transmission: synthesis, packaging, release, action at the target site(s), and termination of the chemical signal. The activity summarizes the major mechanisms by which terminated in the synapse (e.g., reuptake into the presynaptic neurotransmitter action is terminal via membrane-bound transporters, enzymatic degradation in the synapse, simple diffusion), then presents sets of figures depicting fictional datasets that provided information about "mystery neurotransmitters" and novel drugs. Students worked in small teams to analyze these figures and evaluate which mechanism(s) applied to each neurotransmitter or drug.



*Figure 2.* Students' responses to the structure and presentation of the activity. Data are presented as mean +/- SEM. <sup>1</sup> denotes questions that were negatively worded and reverse-coded for analysis and presentation.

The activity was presented like an interrupted case study, with small groups of students working together to collaborate on approaches/answers to the activity questions before sharing their thinking with the class. Instructors could also employ a modified jigsaw technique, where students work in small teams on one part of the activity and then are reassigned to new teams to share their first teams' thinking and answers (Barkley, 2010), asking students to report their group's findings out to the class (Armbruster, 2009) or even

	Points earned			
	Declarative knowledge questions	0	1	2
Short answer	1. What is a synapse? Provide a brief definition here.		12.5%	81.3%
	<ol><li>What are two potential factors that might contribute to a neurotransmitter's action at a given synapse?</li></ol>		20%	73.3%
	<ol> <li>Drugs can prolong a neurotransmitter's action at a synapse. Briefly describe one way that a drug might do this.</li> </ol>	6.3%	0%	94%
True/False	<ol> <li>Neurotransmitter action depends, in part, upon how quickly it is removed from the synapse</li> </ol>		81.3%	-
	5.In general, all synapses contain similar types of structures on the pre- and post-synaptic membranes	25%	75%	-
	<ol><li>Drugs of abuse act on the same exact structures in all synapses.</li></ol>	0%	100%	-
	7. The danger (e.g., abuse liability) of a drug does not really depend upon its action at the synapse.	0%	100%	-
	8. Drugs can alter how neurotransmitters are released and/or removed from the synapse	0%	100%	-

*Table 2.* Students' performance on declarative knowledge questions in the quiz. Data are the percentage of participants in each category.

assigning the activity as homework (Jensen et al., 2015). However, students perceive group work to deepen their learning, promote understanding, stimulate new thinking, and offer helpful perspectives (Gokhale, 1995; Olivares, 2005; Lo, 2010). In the present study, students reported that they believed they benefited from working with others on this activity (Figure 2) and, in their qualitative feedback, that working with other students was one of the most enjoyable aspects of the activity. While students self-assorted into small groups depending on where they were sitting in class, it might be better to pseudorandomly assign students to teams so that they included a range of skills and academic levels. For instance, depending on the instructor's familiarity with her class, it might be useful to assign students based on the reason for enrolling in the course (e.g., specific interest in neuroscience versus fulfilling a major requirement) and/or by academic year (e.g., at least one upperclassman per group).

This activity is flexible enough to be used, in full or in part, in science courses of different sizes, levels, and disciplines. The activity is ideal for use in introductory courses in psychology, biology, or neuroscience that cover synaptic transmission. However, upper-division courses in molecular biology, physiology, and/or pharmacology might also use this activity to review and/or practice applying key concepts. For instance, pharmacology-based courses could use Part 2 of this activity to introduce the general idea of drugs' action at the synapse at the beginning of the semester, or could incorporate this specific example into a unit on psychostimulants.

A major goal of this activity was to introduce the idea that endogenous neurotransmitters allow chemical communication between neurons (Part 1). Instructors could further develop this goal by preparing mini-lectures focusing on different naturally occurring neurotransmitters (e.g., endorphins and opioid receptors) and/or on how learning processes can alter synaptic strength (e.g., long-term potentiation) and how such modifications alter existing neural networks. A second goal of this activity was to emphasize the variety of ways by which exogenous drugs can alter normal chemical communication (Parts 1-2). This section also lends itself to a psychopharmacology minilecture. For instance, I drew connections between the mechanisms of action of the two novel street drugs on dopaminergic synapses, and actual drugs that have similar mechanisms of action (e.g., cocaine as an inhibitor of the dopamine transporter). This portion of the activity, though brief, was memorable to the students, given the nature of their feedback about their learning (see Student Responses). Depending on the goals of the unit/course, an expanded lecture on relevant empirical research on specific reuptake inhibitors (e.g., Sora et al., 1998) could be incorporated into this unit.

Illicit drugs are a common part of many college students' direct or indirect life experience. College students and 12<sup>th</sup> graders have the highest annual prevalence of illicit drug use (39%) out of any age group studied (Johnston et al., 2015, 2016), and most college students report easy access to and opportunities to use illicit drugs (Arria et al., 2008; Garnier-Dykstra et al., 2012). As Feinstein (2010) argues, science literacy involves learning how to draw connections

between scientific concepts and experiences/ideas relevant to your daily life. Critical thinking activities that incorporate key concepts related to drugs of abuse may be more likely to be remembered by college students, but also convey a larger, more important reminder that science can inform situations and topics that students encounter in everyday life (Roberts, 2007).

The ability to read and interpret data and figures is a crucial skill for students interested in scientific and medical careers to hone (AAMC-HHMI, 2009; AAAS, 2010; AAMC, 2010). In the undergraduate classroom, it is valuable to provide opportunities to practice this skill outside the context of primary, empirical research articles, which can be unwieldy and/or intimidating to students, particularly in introductory courses. One of the most challenging aspects of this activity was utilizing the information on both graphs (intra- and extracellular concentrations) to gain insights into the data. Once students caught on to how to approach the information on these graphs, (i.e., that each individual graph did not provide sufficient information to answer the question and that both graphs in the set must be looked at together), the activity seemed to gain momentum and students were able to apply their understanding of the different mechanisms to interpret the information on the graphs. A few teams that appeared "stuck" overheard nearby groups discussing their approach and asked them for help; groups that asked me for help were able to move forward quickly on the limited advice to use the information on one graph to help interpret the other graph in the set. It might also be beneficial to assign students to groups so that each group contained at least one student with some experience reading graphs/figures that could help guide her group's thinking.

It is also worth mentioning that the quiz questions addressed more lower-order learning outcomes (Bloom, 1956) than would have been ideal. This choice was made, in part, to minimize overlap with course exam questions. Assessing students' performance on exam questions was not possible, as participant privacy could not be maintained given the relatively small size of the class. Future work might consider including an option for students to submit their answers to relevant exam questions; this would also likely reduce selection bias in the present sample. Asking different types of questions on the study guiz and course exams did reduce the risk that study participants would gain an unfair advantage on future exams. It is also generally difficult to collect valid, thoughtful answers to higher-order questions on an anonymous quiz, for which participants are not compensated differently based on their accuracy or thoughtfulness but rather only on guiz completion. Given these limitations, students did well on the declarative knowledge portion of the study, suggesting that they learned and retained the major points of the activity.

Overall, this activity offers students an opportunity to develop key scientific competencies, think critically about data, and collaborate with peers on questions related to synaptic function and neurotransmission. These topics are cornerstones of undergraduate neuroscience curricula and this activity could be used in a range of undergraduate neuroscience, psychology and biology courses.

The *"Mystery Neurotransmitters"* activity is available as supplementary material to this article. For a copy of the key and/or to discuss ideas for its implementation, please contact the author.

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