Neuro 405
Spring 2023
Sherlock Holmes Project

The Case of the Four Toxins

(*adapted from Adler and Schwartz, 2006*)

Case Details

It had been a bleak and foggy November in the year 1906. All London was horrified by the deaths of Mr. David Small, Mrs. Violet Mason, and Mr. Benjamin Marinus,. All three had been found in their homes, dead of respiratory failure secondary to paralysis of the muscles of the chest and thorax. Discarded vials containing solutions, which experimental analysis showed caused paralysis in toads, were found in the vicinity of all three murder victims.

Chemical analysis indicated that the toxic component in each solution was unidentifiable by forensic science. Very strong circumstantial evidence, uncovered by Mr. Sherlock Holmes, linked 25-year-old Jack Ferguson, who recently returned from traveling abroad, to the death of Mrs. Mason. However, Ferguson was being detained by the police at the time Mr. Small and Mr. Marinus were murdered and therefore cannot have been responsible for their deaths.

Inspector Lastrade felt that it was impossible that more than one unknown poison could have the identical effect and that more than one person in London could have managed to obtain such an obscure poison at the same time. He therefore felt that Ferguson could not have been guilty of the death of Mrs. Mason. Sherlock Holmes questioned the assumption that all three poisons had the identical effect.

"When you have eliminated the impossible," he said, "whatever explanation remains, no matter how improbable, must be correct. Is it not possible that three different toxins, acting in three completely different ways, all have the same final result of paralysis? In that case, it would be more likely that the murders were committed by multiple individuals than by the same person."

"Nonsense," said Inspector Lastrade, "Paralysis is paralysis. How could three different toxins acting in completely different ways all have the same final effect?" On this basis, Ferguson is freed.

In discussing the case with Dr. Watson, Sherlock Holmes shook his head, "Time will prove me right, Watson," he said, "I feel quite certain. If only we knew more about neuromuscular physiology…" He sighed deeply and reached for his violin.

Your Assignment

A group of 7 neurophysiologists has been called in to help Mr. Holmes and Inspector Lastrade with the investigation. The group has been divided into teams and assigned to the three murders like so:

Lab Teams:

Mr. D. Small	**Mrs. V. Mason**	**Mr. B. Marinus**
Student 1	Student 4	Student 6
Student 2	Student 5	Student 7
Student 3		

The teams are to assume they have access to all modern electrophysiological tools and procedures. The goal is to design experiments to figure out what toxin was used in each murder, or at least to narrow down the list considerably! The teams should use today as a research day. You will need to be familiar with some basic recording techniques and the organization of the neuromuscular junction (which we will be covering in class in a few weeks). **Your assignment:** find information on the following topics (from books, the internet, the library, etc.): **extracellular recording, two-electrode voltage clamp, patch clamp, the neuromuscular junction (NMJ), and one additional topic that your group thinks may be useful.** As a group, write a paragraph or two on each subject to 1) use as a reference when you start designing experiments and 2) show me what you have learned on the topics. Be sure to include citations of any references you use, and write everything in your own words. This 1-2 page paper (a single paper per group) will be due by the end of class on **Jan. 26**. I recommend starting a Google Doc that you can add to and revise throughout the semester. Please name your document like this: **SH_2023_VictimName_Name1_Name2_Name3** (i.e. the first names of your group members)

For each e-phys technique, please include the following:

1. A general big picture of how the technique works.
2. The types of questions/topics that are studied the technique (at least 2 examples).

For the NMJ, please include the following:

1. A description of the structure (i.e. what is the NMJ), highlighting important elements.
2. What specific type of receptor is found at the NMJ, and how does it work to help promote muscle contraction?

On **March 2**, we will use the lab period to organize and decide on a plan of attack, as it were; the teams will formulate their Preliminary Plans, which will be submitted at the end of class. After receiving the results of the first experiments, there will be another lab period (**March 23**) to allow the teams to formulate a second experiment. This pattern may be followed outside of class for an optional additional round (due April 7).

Toward the end of the semester, each team will formulate its conclusions, and make a final presentation to the class on **April 27**. A single write-up of the team's findings will be submitted on **May 1** (the last day of classes). The written report should discuss what conclusions the team made on the case, and explain how they arrived there. It should be about 3 pages, and must incorporate at least three references from the scientific literature, cited appropriately. There will also be **points for creativity**- in the

presentation as well as the report (it can be the same creativity plan for both parts of the project)- have fun with this!

NOTE: if any group member is not in class or otherwise does not do their fair share of the work, Dr. French must be notified. If the labor becomes too inequitably divided, the relevant partner may be removed from the group and will have to complete the project on their own.