NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

All or Nothing: A Case Study in Muscle Contraction

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Part I – The Tour

You are an intern working in the Atlanta, GA office of Dr. Priya Wayne, MD. Dr. Wayne is a specialist in rare neuromuscular and musculoskeletal disorders. You've been working with Dr. Wayne for the last year and due to this experience you've gained a great deal of knowledge about the human body and muscle physiology. You're also a college student and working with Dr. Wayne has allowed you to gain first-hand experience with some of the material that you're learning in your human physiology course. Just last week you had to turn in an assignment comparing and contrasting disorders of the neuromuscular junction. You learned all about several issues, including myasthenia gravis, sarin, curare, botulism, and Eaton-Lambert syndrome.

Today a group of high school students is coming for a tour and Dr. Wayne has asked you to prepare some information about muscles to present to the students. Specifically, Dr. Wayne has asked you to discuss the neuromuscular junction (NMJ), skeletal muscle contraction, and explain some of the issues that can occur when signaling between neurons and muscles does not go as planned.

Questions

Use the word bank to match the appropriate letter to the definitions/descriptions on the next page.

(a) Sodium	(i) Synaptic vesicles
(b) Nicotinic acetylcholine receptor (nACh)	(j) T-tubule
(c) Myosin	(k) Sarcoplasmic reticulum
(d) Actin	(l) Dihydropyridine receptor
(e) Acetylcholine (ACh)	(m) Ryanodine receptor
(f) Depolarization	(n) Synaptic terminal
(g) Motor end plate	(o) Sarcolemma
(h) Acetylcholinesterase (AChE)	(p) Sarcomere

*These four undergraduate students contributed equally to the creation of this case study and are listed in alphabetical order.

1. ___ Thin contractile protein involved in cross-bridge formation, comes in filamentous or globular forms.
2. ___ Store neurotransmitters, and following a Ca^{2+} driven signal, dump neurotransmitters into the synapse.
3. ___ The structure at the end of the axon that contains neurotransmitters and vesicles.
4. ___ The functional unit of the muscle fiber that includes the A-band, I-band, H-zone and the M-line.
5. ___ The ion responsible for depolarizing the muscle membrane by traveling through the nACh receptor, down its electrochemical gradient.
6. ___ Located on the sarcoplasmic reticulum and once opened, allows Ca^{2+} flow from the sarcoplasmic reticulum into the sarcoplasm.
7. ___ Thick filamentous contractile protein involved in cross-bridge formation, has a club-like appearance with a "head."
8. ___ A neurotransmitter derived from choline; responsible for sending the excitatory signal in the neuromuscular junction.
9. ___ These invaginations allow depolarization of the muscle membrane to quickly penetrate from the sarcolemma to the myofibril.
10. ___ Large and complex terminal formation by which an axon of a motor neuron establishes synaptic contact with a skeletal muscle fiber, transmitting neural impulses to a muscle.
11. ___ The plasma membrane of a muscle fiber.
12. ___ The enzyme responsible for stopping the ACh signal. Functions by metabolizing ACh into choline, which is recycled, and acetate.
13. ___ Responsible for opening a ligand-gated Na^+/K^+ channel in the muscle membrane when the proper ligand binds to it.
14. ___ A L-type calcium channel in the muscle cell membrane, activated upon depolarization, couple depolarization signal to release of calcium.
15. ___ An electrical change which brings the relative charge of the inside of the cell more positive; necessary for transmission of electrical impulses within a cell, or from one cell to another.
16. ___ Modified endoplasmic reticulum, stores and releases calcium.

Exercise

Using the sliding filament theory, explain (or draw) the process of sarcomere shortening. Start from the point where calcium would interact with troponin. Make sure to discuss the roles of actin, myosin, and ATP.

Part II – Jeff Slater

After the high school group finishes their tour, Dr. Wayne sees two patients.

Jeff Slater is a biochemist working for a biowarefare lab at the CDC. He is currently working on a project to develop a new neurotoxin and is using sarin as a model substance. Suddenly while working the lab alarms go off and Jeff accidentally knocks a vial of sarin over and a bit of the liquid splashes onto his arm between his gloves and lab coat. He suddenly starts to feel dizzy, his heart starts pounding harder than ever, and he has shortness of breath. He feels incredibly sluggish and tries to get to the exit. As he approaches the lab door, his muscles cramp up and he falls down and hits his head, knocking him unconscious. His colleague from across the hall happens to see him fall and calls for help. Jeff is given oxygen and taken to the nearby hospital, which happens to have a neuromuscular specialist. The sounding of the alarm turns out to have been just routine testing of a new system.

Questions

1. What symptoms is Jeff experiencing?

2. What is the role of AChE in the NMJ?

Jeff is admitted to the hospital and Dr. Wayne examines him. Jeff is unconscious but seems to be experiencing some paralysis, so Dr. Wayne orders blood work. Results are listed below.

J. Slater – Test Results

Test	*Result*	*Normal Range*
Blood Pressure	105/65	90-120/60-80
Hematocrit (%)	37.5	36-38
Glucose (mg/dl)	88	70-110
Sodium (mmol/L)	139	135-145
Potassium (mmol/L)	3.8	3.5-5.0
AChE Activity Test (%)	44	100
Tetraiodothyronine or thyroxine (T_4) (ng/dL)	9.1	4.6–12
Serum Triiodothyronine (T_3) (ng/dl)	112	80–180
Antibodies for Ach Receptors	Not Present	Not Present

Dr. Wayne looks over the results and knows from Jeff's colleague that he is a bioweapons biochemist. Dr. Wayne figures out that Jeff has been working on synthesizing a new sarin-like biochemical weapon and suspects Jeff has a type of poisoning that is similar to that of sarin.

Questions

3. Which of Jeff's levels are abnormal?

4. What is the mechanism of action of sarin or a sarin-like chemical?

5. How would exposure to a sarin-like poison affect the amounts of Na^+ going into the muscle cell? Explain why.

6. How would exposure to a sarin or sarin-like chemical affect Ca^{2+} levels inside the sarcoplasmic reticulum? Why?

7. How do these altered Ca^{2+} levels affect the position of the actin and myosin filaments? Why/how?

8. What needs to happen to Jeff's post-synaptic membrane to remedy his paralysis? Physiologically what do we need more of, and where?

Part III – Sandy Thompson

A 25-year-old preschool teacher, Sandy Thompson, has not been feeling like herself lately. She has been feeling quite tired and her co-workers have commented on her droopy eyelids. Additionally, she is experiencing weakness in her arms and legs, has difficulty talking clearly and even her students' parents have been concerned that Sandy hasn't been looking very happy at work. One day at lunch, Sandy started to choke on her food, causing one of her coworkers to perform the Heimlich maneuver on her. While the scare didn't cause any permanent damage, Sandy is convinced that it is time to go see a doctor.

When she finally arrives at her appointment with Dr. Wayne, she explains to Dr. Wayne what has been going on, and the doctor decides to run a few blood tests. Sandy's blood work results are presented below.

S. Thompson – Test Results

Test	*Result*	*Normal Range*
Blood Pressure	115/73	90-120/60-80
Hematocrit (%)	36.5	36-38
Glucose (mg/dl)	94	70-110
Sodium (mmol/L)	144	135-145
Potassium (mmol/L)	4.3	3.5-5.0
AChE Activity Test (%)	100	100
Tetraiodothyronine or thyroxine (T_4) (ng/dL)	11.3	4.6–12
Serum Triiodothyronine (T_3) (ng/dl)	154	80–180
Antibodies for ACh Receptors	Present	Not Present

Questions

1. What symptoms is she experiencing?

2. What levels from her blood work are abnormal?

3. How would antibodies against ACh receptors affect the neuromuscular junction?

4. How would antibodies against the ACh receptors affect the influx of Na^+ into the cell?

5. How would antibodies against the ACh receptors affect the levels of Ca^{2+} inside the sarcoplasmic reticulum? What effect does this have on the actin and myosin filaments?

6. What disorder does Sandy have? How do we treat/manage this diagnosis?

7. Using the below table, compare the muscle contraction problems faced by Jeff and Sandy to that of a normal person. Use normal, increased, decreased to complete the table.

	ACh	*AChE*	*ACh Receptors*	*Na^+ influx*	*SR Ca^{2+} release*	*Cross bridge formation*	*Frequency of muscle contraction*
Healthy person							
Jeff							
Sandy							