Biological and Biochemical Foundations of Living Systems

See examples from each of the four sections of the MCAT Exam. The passage in each example provides the context for the questions. The correct answer is provided as well as an explanation that refers to the Foundational Concepts and skills tested.

Passage

The myocellular transmembrane Na^+ gradient is important for proper cellular function. During septic shock, disruption of Na^+ homeostasis often occurs and leads to decreased membrane potential and increased intracellular Na^+. It has been found that failure of cellular energy metabolism is a common symptom in septic patients who do not respond to therapeutics. Because normal intracellular levels of Na^+ are maintained by the Na^+K^+ ATPase, it is important to understand how metabolic energy production is linked to cation transport.

Researchers are interested in whether the energy used for ion transport is derived from glycolysis or oxidative phosphorylation. This information would provide a better understanding of myocellular damage that occurs during critical illness. Experiments were conducted to evaluate the effects of glycolytic inhibition on cellular Na^+ and K^+ concentrations and lactate production in rat skeletal myocytes.

Rat skeletal muscle fibers were extracted and incubated in normal media (control), glucose-free media (G(−)), and glucose-free media with various concentrations of the glycolytic inhibitor iodoacetate (IAA). IAA directly prevents the formation of 1,3-bisphosphoglycerate. After one hour in the media, the muscle tissues were assayed for intracellular Na^+ and K^+ content and lactate production. Cellular viability was determined by measuring the amount of lactate dehydrogenase (LDH) released, as LDH release is an indicator of cell death. The results are displayed in Figure 1.

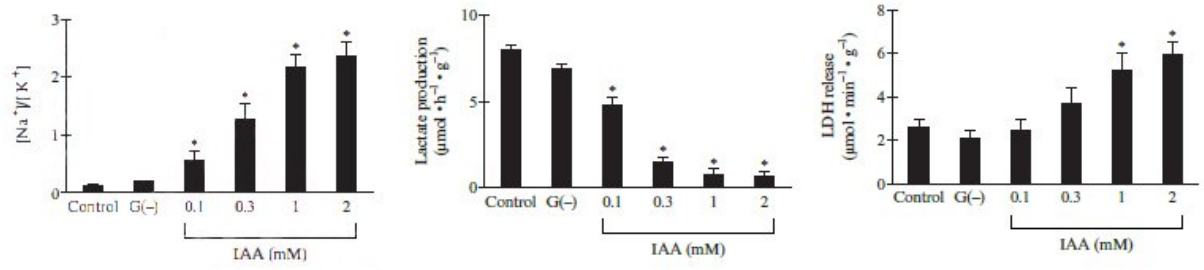

Figure 1 Effects of glycolytic inhibition on intracellular Na^+ and K^+ content and lactate production with cellular viability measured by LDH release. (Note: The * indicates $p < 0.05$ versus control.)

The researchers also examined the effect disruption of oxidative phosphorylation had on Na^+ and K^+ content. Inhibition of oxidative phosphorylation was caused by carbonyl-cyanide m-chlorophenylhydrazone (CCCP), an ionophore that allows protons to move freely through membranes. No correlation between Na^+ and K^+ content and oxidative phosphorylation was found.

Adapted from: Okamoto K, Wang W, Rounds J, Chambers EA, Jacobs DO. ATP from glycolysis is required for normal sodium homeostasis in resting fast-twitch rodent skeletal muscle. *The American Journal of Physiology-Endocrinology and Metabolism*. 2001 Sept;281(3):E479-88.

Questions:

1. The researchers chose a concentration of 0.3 mM IAA as the working concentration for any additional studies instead of 1 mM or 2 mM. What is the likely reason for this?

A) The lower concentration of IAA gave the largest Na^+ response.

B) Higher concentrations induced significant cytotoxicity.

C) The solubility of IAA was not high enough.

D) The researchers were trying to mimic control conditions as closely as possible.

Answer

Correct Answer is B) Higher concentrations induced significant cytotoxicity.

Rationale: This question requires the test taker to apply knowledge about cytotoxicity and cell lysis to the design of an experiment described in the passage. In particular, the examinee should understand that conducting an experiment where the level of IAA was cytotoxic to the cells (when compared to control conditions) would not be desirable for understanding the role of glycolysis in establishing ion concentration gradients, as these cells would lose membrane integrity and undergo lysis. Therefore, the experimental design should not use an IAA concentration that results in significantly increased cell lysis.

2. The information in the passage suggests that glycolysis:

A) is important for maintaining normal Na^+ and K^+ levels in skeletal muscle.

B) facilitates membrane permeability in skeletal muscle.

C) impedes the function of the Na^+ and K^+ ATPase in skeletal muscle.

D) is regulated by the Na^+ and K^+ ATPase in skeletal muscle.

Answer

Correct Answer is A) is important for maintaining normal Na^+ and K^+ levels in skeletal muscle.

Rationale: This question requires the test taker to apply knowledge about glycolysis to the experimental data from Figure 1. In particular, the trend in the data that shows increasing concentration of IAA results in a higher ratio of the concentration of Na^+ to K^+ than observed in the control sample must be correlated with role of IAA in the disruption of glycolysis. This is further supported by the drop in lactate production shown in Figure 1 at higher concentrations of IAA, because IAA prevents the formation of NADH, which is used when pyruvate is reduced to lactate. The combination of the proposed role of IAA and the results from Figure 1 lead the test taker to the conclusion that glycolysis is important to the Na^+K^+ ATPase and, therefore, important to the maintenance of the concentration ratio of Na^+ to the K^+.

3. If the effects of IAA treatment in nerve cells are the same as those observed in myocytes, which feature of an action potential would be most affected by IAA treatment?

A) Initiation of depolarization

B) Rising phase of depolarization

C) Falling phase to undershoot

D) Return to resting potential

Answer

Correct Answer is D) Return to resting potential

Rationale: This question requires the test taker to recall information about the role of the Na^+K^+ ATPase in the recovery of the nerve cell resting potential after an action potential. In addition, the test taker must reason about the effect of IAA treatment based on the information presented in the passage, and how the inhibition of glycolysis by IAA would affect the cellular concentration of ATP. Based on these two lines of reasoning, the test taker can propose a hypothesis about which portion of an action potential would be affected by IAA treatment.

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655 K Street, NW, Suite 100 Washington, DC, 20001-2399