

Cellular Mechanism of Fatigue

pH during exercise goes down as we accumulate H^+ from metabolism
(Lactate and pyruvate)

-Protons can be detected by nociceptors and contribute to the “burn”

pH and lactate are not =

>Lactate is good, it does not contribute to acidosis, but helps delay the buildup of protons. Lactate is good during exercise for energy

In the presence of elevated proton concentrations:

1. SR/ Ca^{2+} kinetics affected

2. Contractile unit can be obstructed (weaken cross-bridge)

As Ca^{2+} leaves the SR, H^+ sneak in

When Ca^{2+} comes in, H^+ gets pushed out.. works great under ‘normal’ conditions. Room for error*

>troponin C sensitivity to Ca^{2+} and cross-bridge cycling result in impaired muscle force

-During exercise, muscle cells lose potassium (positive charge)

-Excitability of the cell decreases (lower charge)

-Action potential diminishes

-Buildup of H^+ , the potassium loss continues but the t-tubules become less permeable to chloride (negative charge)

-If negative charge stops sneaking in, membrane potential is better preserved

Less inhibition = more excitability

Phosphates

>Come from ATP hydrolysis

-Possible that it decreases myofibrillar calcium sensitivity

Remember:

You have to release the phosphate to create a strong bond

-High concentrations of phosphate in the muscle hinder the release of phosphate from myosin, leaving cross-bridge in a weak bond state

>Chloride channels are permeable to phosphates (when ATP levels are low) and binds to calcium (problem: you’re unable to release calcium, which is needed to bind to troponin C)

Magnesium

>As levels of ATP decrease, levels of free Mg^{2+} rise

- Mg^{2+} affects RyR and competes with Ca^{2+} for binding to the activation sites; impairing calcium-regulated function of the RyR

ROS

>Free radical with oxygen in it

-Premature leaked electrons, creates superoxides and affects fatigue

(The more you exercise, the more superoxide you generate)

>Lipid peroxidation (stealing electrons from cell membranes; mostly arachidonic acid)

>Hydrogen peroxide impair the depolarization-induced calcium release

>Sodium potassium pump dysfunction during exercise

Local Inflammation

Heat

> Alters enzymes, hemoglobin, electrolyte balance, reduced SV, increased HR

Glycogen Availability

> Blood Glucose drops and efficiency drops