Does Only the ?2 Subunit of the Na+, K+-ATPase in Skeletal Muscle Respond to Stimulation By Epinephrine?

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After trauma or hemorrhage, blood levels of both Epinephrine (Epi) and lactate rise. Traditionally, hyperlactatemia is interpreted as anaerobic glycolysis secondary to tissue hypoxia. However, Epi stimulates Na+, K+-ATPase activity in muscle linked to aerobic glycolysis. Skele-tal muscle has two isoforms of the catalytic ? subunit of the Na+, K+-ATPase, ?1 and ?2. These isoforms may have distinct functions if one isoform (? 1) maintains the basal intracellular Na+, K+ ratio while the other (?2) responds to hormones during stress. Pumps with the ?2 isoform may be selectively stimulated by Epi, thus increasing, ATP utilization and aerobic glycolysis. The ?2 isoform is inhibited by a lower concentration of ouabain (10-6M) than ?1 (10-3M). If Epi stimu-lates ?2 selectively, then Epi-stimulated lactate production and fall in intracellular Na+/K+ ratio should be inhibited at low ouabain concentration. METHODS: Bilateral extensor digitonim longus (EDL) and soleus muscles of Sprague-Dawley rats (45-55 grams) were dissected, with one muscle being treated with a range of ouabain concentrations (10-6 -10-3 M) and the untreated, contralateral muscle as the control. Half of the muscles were treated with Epi. Lactate produc-tion, intracellular Na+/K+ ratio and glycogen were measured. RESULTS: Selectively inhibiting the ?2 isoform (10-6M) increased the Na+/K+ ratio, preserved glycogen levels, and decreased lac-tate production, as compared to controls. Inhibition of all pumps (I 0-'M ouabain) caused a fur-ther increase in the Na+/K+ ratio and glycogen level, and decrease in lactate production. CONCLUSIONS: The ?2 isoform predominantly responds to Epi, but there is some stimulation of the ?1 isoform by Epi as well. These results further link Epi and the Na+, K+-ATPase to in-creased lactate production in trauma and hemorrhagic shock.