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The Effect of Shear Stress, Potassium, and Adenosine on α-1 Adrenergic Vasoconstriction of Rat Soleus Feed Arteries

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INTRODUCTION

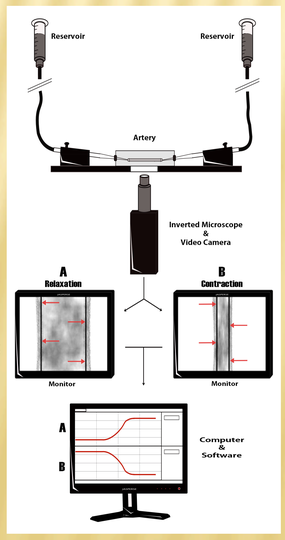
During exercise, blood flow increases to the working skeletal muscle primarily because of dilation of the arteries and arterioles feeding the muscle. Sympathetic nerve activity also increases during exercise, augmenting the release of the neurotransmitter norepinephrine (NE) at the arterial wall and into the blood. NE acts to constrict blood vessels; however, arteries and arterioles within contracting skeletal muscle dilate despite the increased NE present. This has led to the concept of functional sympatholysis (4), the idea that a chemical released from contracting skeletal muscle interferes with NE signaling. NE acts by binding to adrenergic (alpha and beta) receptors, and it is alpha receptors in the arterial wall that cause vasoconstriction (8). While both α-1 and α-2 receptor subtypes have been found in some vascular beds of some species, there is significant evidence that in rat calf muscles, the response to norepinephrine is mediated solely by α-1 receptors (5, 9). Because α-1 receptors are the sole respondents to sympathetic signaling, we studied three proposed substances that may interfere with sympathetic signaling at the α-1 receptors, thereby mediating sympatholysis. There is evidence to suggest that heat and acidosis may partially mediate sympatholysis of α-1 receptors (1, 2). This study sought to determine whether increased levels of shear stress, potassium, or adenosine also contribute to sympatholysis. If shear stress, potassium, and adenosine are, in fact, sympatholytic agents, they will reduce the vasoconstriction mediated by the α-1 receptors in rat soleus muscle feed arteries. We hypothesized that all three variables would be sympatholytic agents.

METHODS

- Rat soleus feed arteries were isolated and cannulated on two glass micropipettes for in vitro video microscopy.
- Feed artery maximal diameter was 199.7 ± 4.7 µm.
- Feed arteries developed a spontaneous tone of 43.7 ± 1.8%.

Artery Set-Up: After cannulation, each artery was incubated for 60 minutes in a 2 mL bath of physiological saline solution as pressure and temperature were gradually increased to in vivo levels. Temperature was set at 37°C and intraluminal pressure was set at 90 cmH_2O to represent pressure found in vivo in soleus feed arteries (11). Artery diameter was measured using video calipers (see image below).

Experimental interventions: Phenylephrine, an α-1 agonist, was added to the bath in half-log concentration increments and a dose-response relationship was obtained. Phenylephrine dose-response curves were obtained under control conditions and in the presence of various levels of shear stress, potassium, or adenosine. Potassium and adenosine were added directly into the 2 mL bath. Shear stress was induced by manipulating the heights of the reservoirs (see image to the right) to introduce flow through the artery. Three levels of each condition were used to represent an estimation of control, low, and high concentrations in the body during exercise (3, 6, 7).



RESULTS

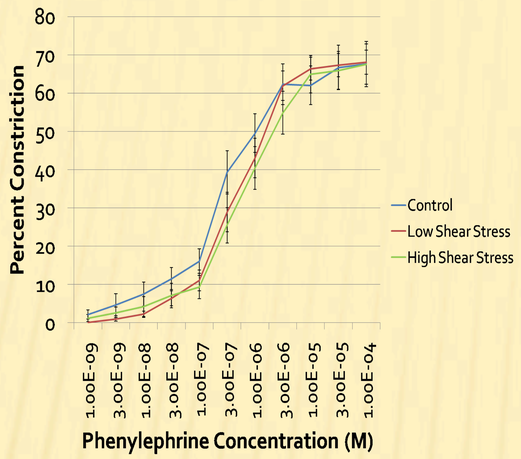


Figure 1: Shear Stress did not reduce constriction to Phenylephrine. Estimated shear stress values of 0 dy/cm², 25 dy/cm², and 135 dy/cm² were calculated for no, low, and high levels of shear stress, respectively (3). (N= 12 arteries from 12 rats)

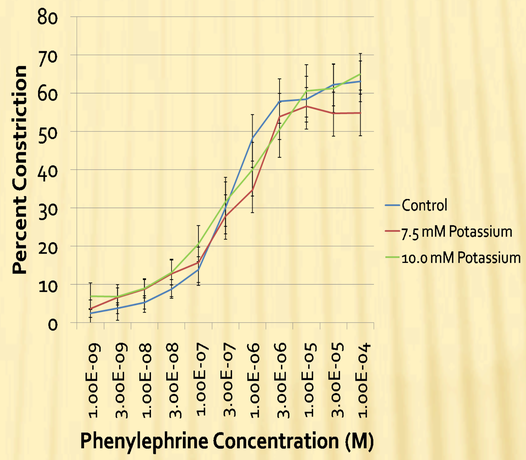


Figure 2: Potassium did not reduce constriction to Phenylephrine. Potassium concentrations of 5 mM, 7.5 mM, and 10 mM represent in vivo concentrations at rest, low-intensity exercise, and high-intensity exercise, respectively (6). (N= 17 arteries from 12 rats)

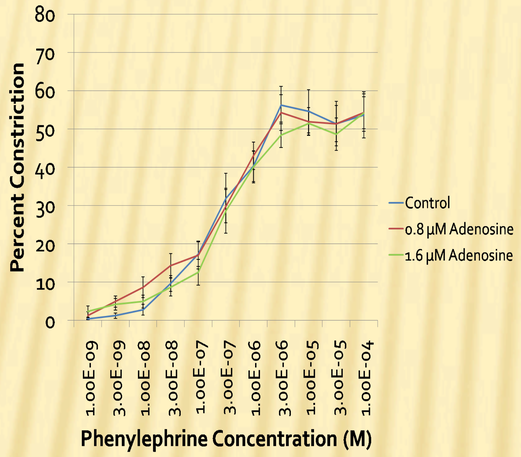


Figure 3: Adenosine (in vivo concentrations) did not reduce constriction to Phenylephrine. Adenosine concentrations of 0 µM, 0.8 µM, and 1.6 µM represent in vivo concentrations at rest, low-intensity exercise, and high-intensity exercise, respectively (7). (N= 12 arteries from 12 rats)

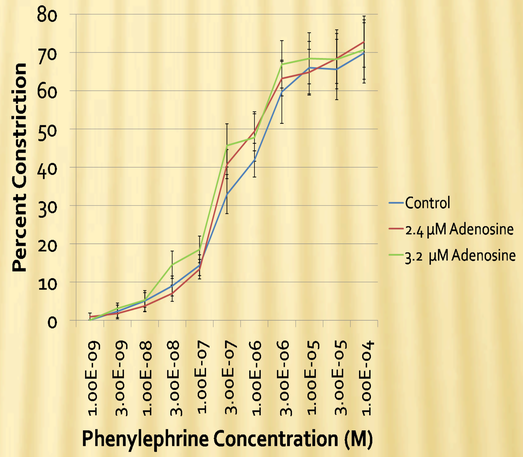


Figure 4: Adenosine (high concentrations) did not reduce constriction to Phenylephrine. Due to the observations in the presence of 1.6 µM adenosine, higher adenosine concentrations were used in another set of arteries. (N= 9 arteries from 9 rats)

DISCUSSION

Our data show no significant difference between α-1 mediated vasoconstriction in the absence and presence of shear stress, potassium, and adenosine. This data is not consistent with that of Ives et al., who found heat and acidosis attenuated sympathetic vasoconstriction of α-1 adrenergic receptors in human arteries (1, 2). However, this data is consistent with the findings of Thomas et al., who found that soleus muscle contraction did not attenuate sympathetic vasoconstriction. Thomas et al. hypothesized that the ability to fight sympathetic constriction may be dependent upon muscle fiber type (10). Because of this literature, our lab is furthering this study of the three proposed sympatholytic agents by carrying out the same procedures on arterioles from the rat gastrocnemius, a predominantly glycolytic muscle, for comparison with the rat soleus, a predominantly oxidative muscle. Furthermore, we have initiated confirmation of acidosis as a sympatholytic agent in soleus feed arteries to determine if the soleus muscle is capable of fighting sympathetic vasoconstriction.

CONCLUSIONS

- Soleus feed arteries respond to sympathetic vasoconstriction via α-1 adrenergic receptors.
- The presence of shear stress, potassium, and adenosine did not reduce vasoconstriction to phenylephrine, indicating that these factors are not sympatholytic in soleus feed arteries.
- Because there is evidence that predominantly glycolytic muscles fight sympathetic vasoconstriction, we are currently examining the effect of the three proposed sympatholytic agents on gastrocnemius arterioles.

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