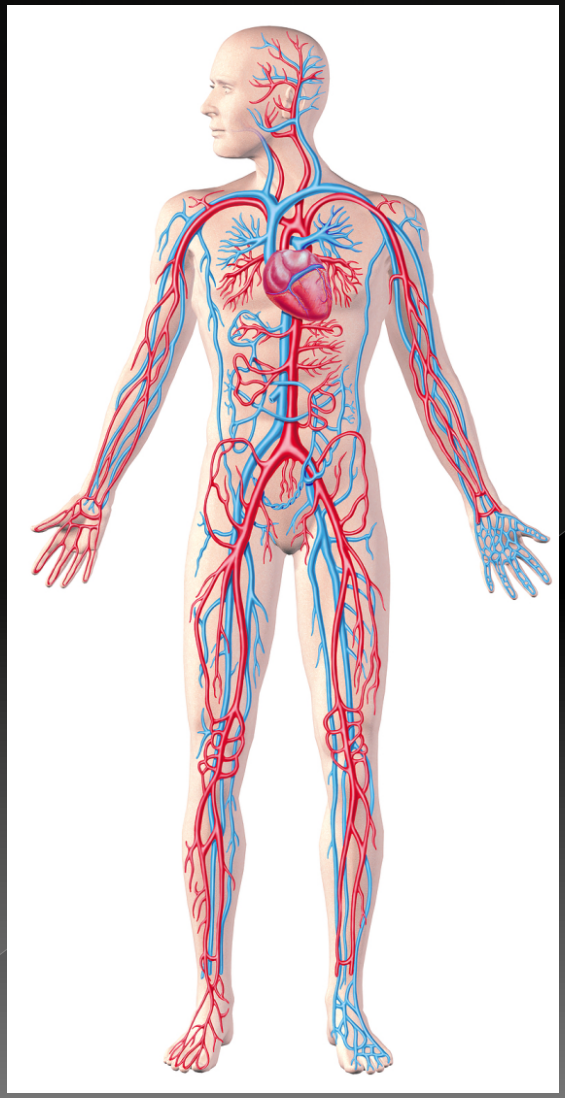
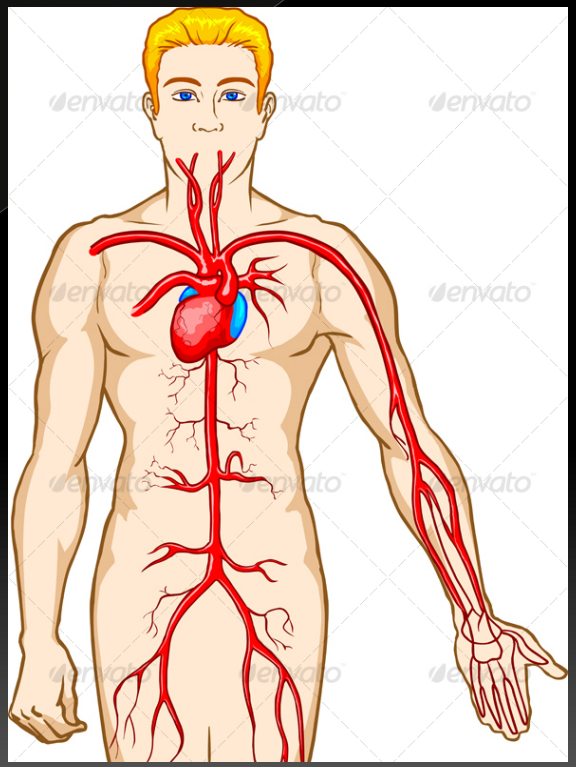
The Effect of Shear Stress, Potassium, and Adenosine on α-1 Adrenergic Vasoconstriction of Rat Soleus Feed Arteries

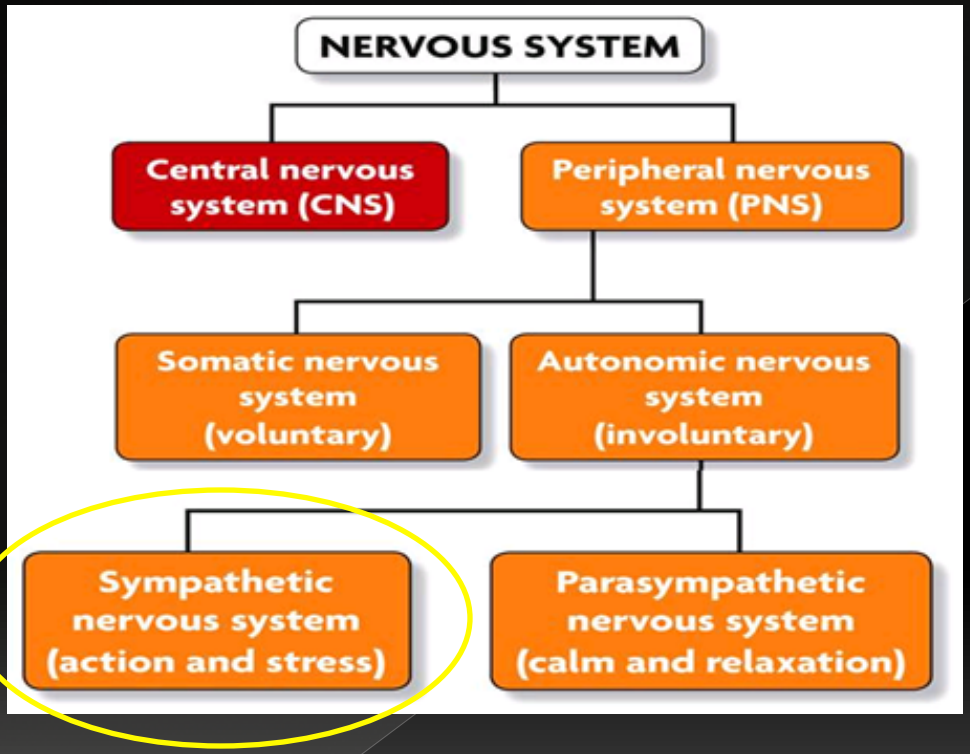
Tanner J. Heckle and Jeffrey L. Jasperse
Pepperdine University, Malibu, CA

Blood Flow

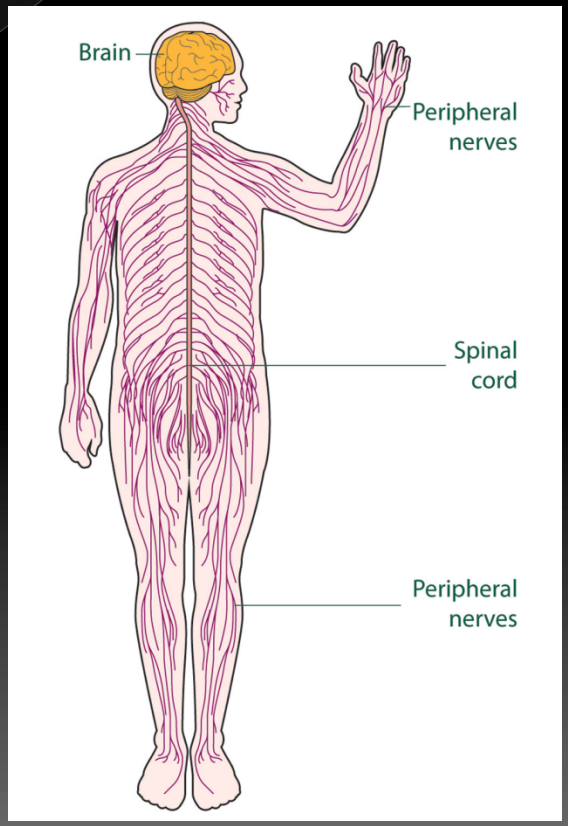




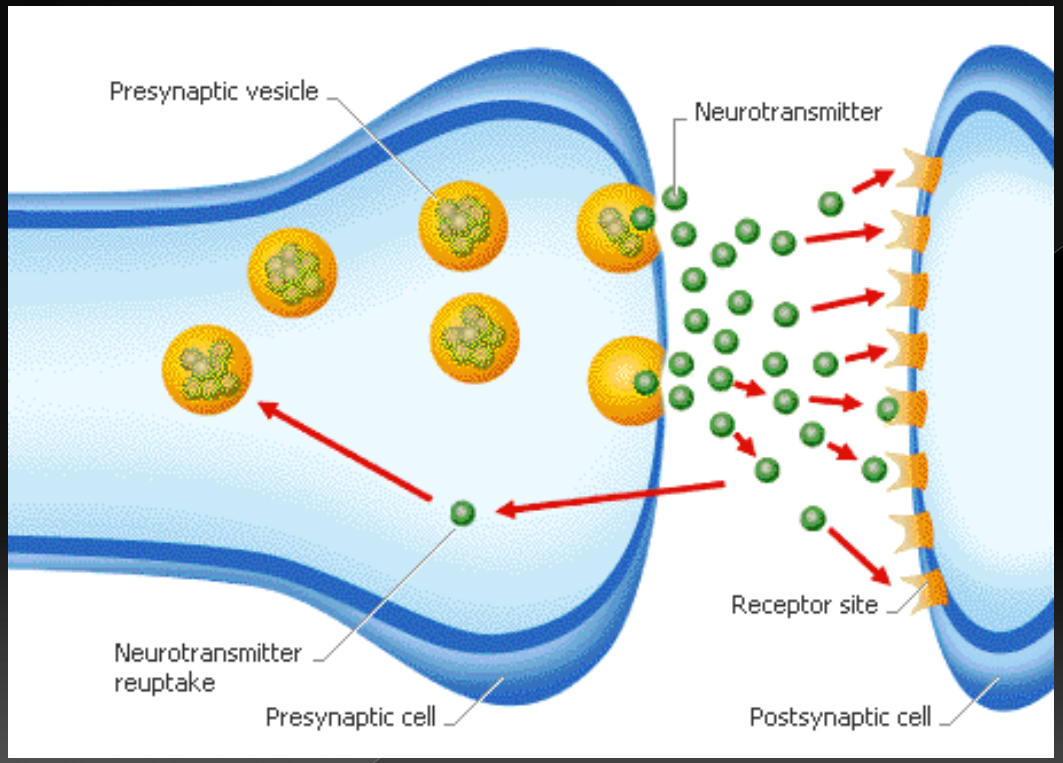
Nervous System



SNA – "Fight or Flight"



Sympathetic Nervous System



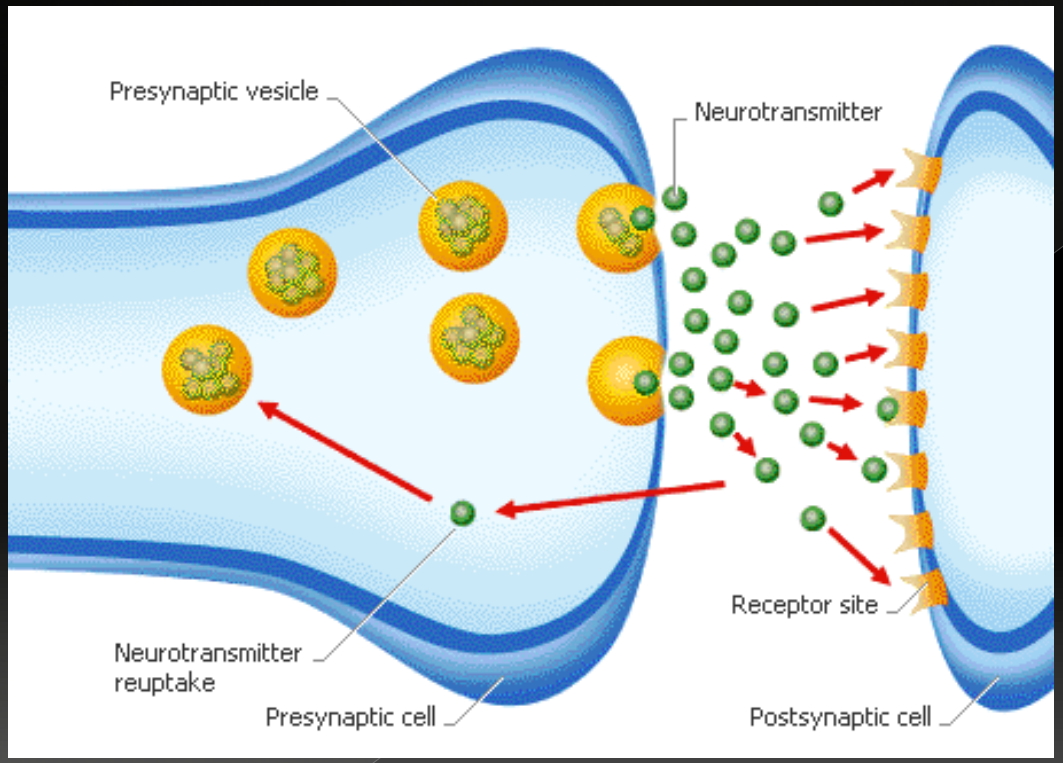
Neurotransmitter:

- Norepinephrine (Adrenaline)

Receptor:

- Adrenergic Subtypes:
  - Alpha (α)
    - α -1
    - α -2
  - Beta (β)
    - β -1
    - β -2

Sympathetic Nervous System



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Sympatholysis

1. Exercise is a fight or flight response.
2. SNA increases during exercise.
3. Norepinephrine (from SNA) constricts arteries.
4. Sympatholysis

   "sympatho" – sympathetic

   "lysis" – breaking

"The responsiveness of the vasculature to sympathetic stimulation diminishes during exercise."

Necessary Characteristics of a Sympatholytic Agent

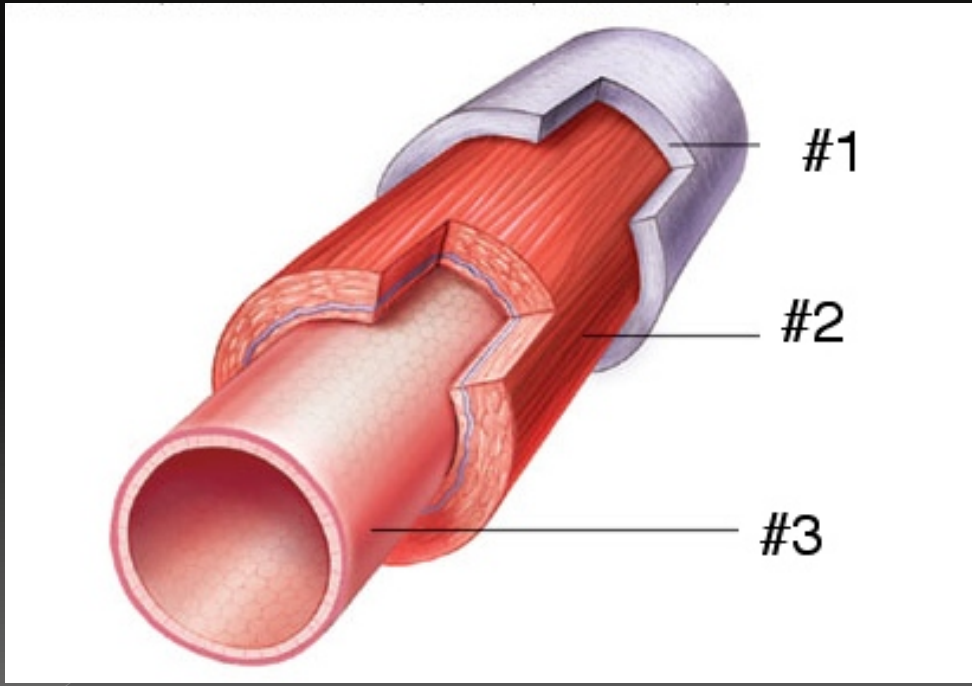
1. Increase during exercise
2. Interfere with Sympathetic signaling

Possible Agents:

1. Acidosis (Ives S et al. J Physiol 2012; 113:1690-1698)
2. Temperature (Ives S et al. Exp Physiol 2012)
3. Shear Stress
4. Potassium
5. Adenosine

Proposed Sympatholytic Agents

1. Shear Stress



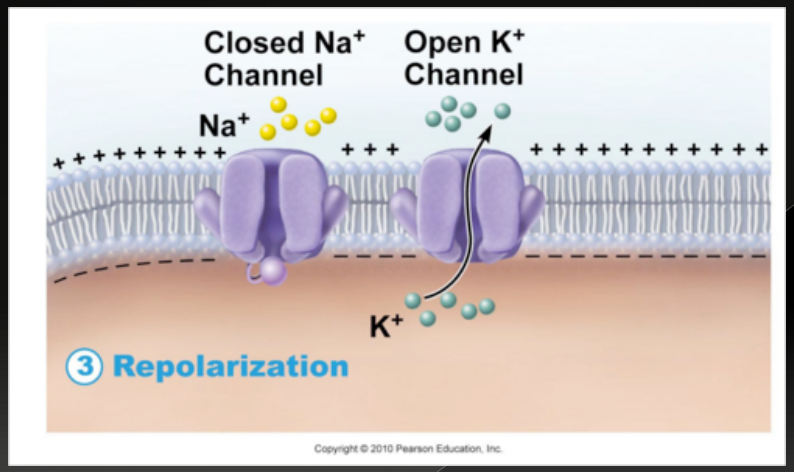
Connective Tissue

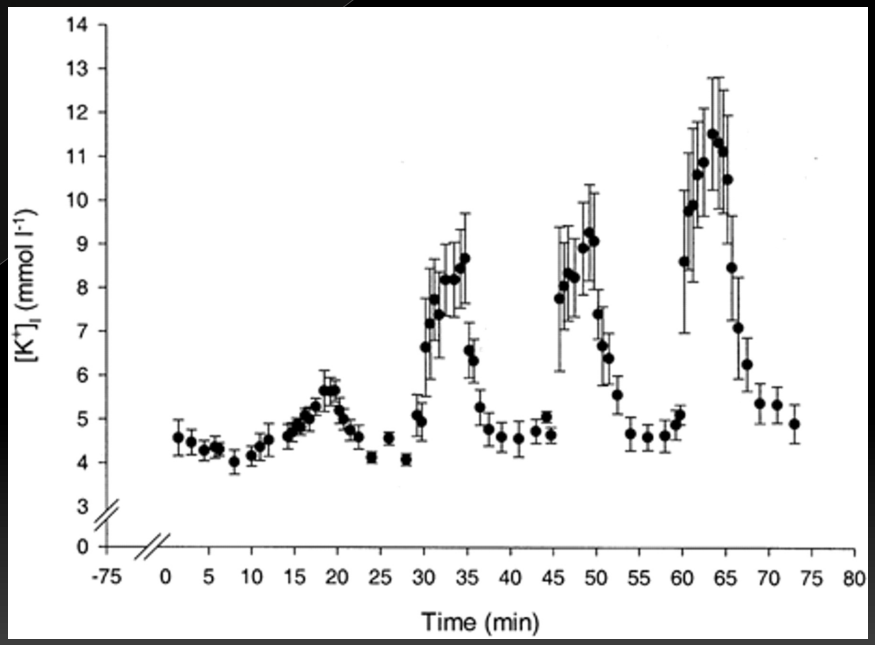
Smooth Muscle

Endothelium

Proposed Sympatholytic Agents

2. Potassium

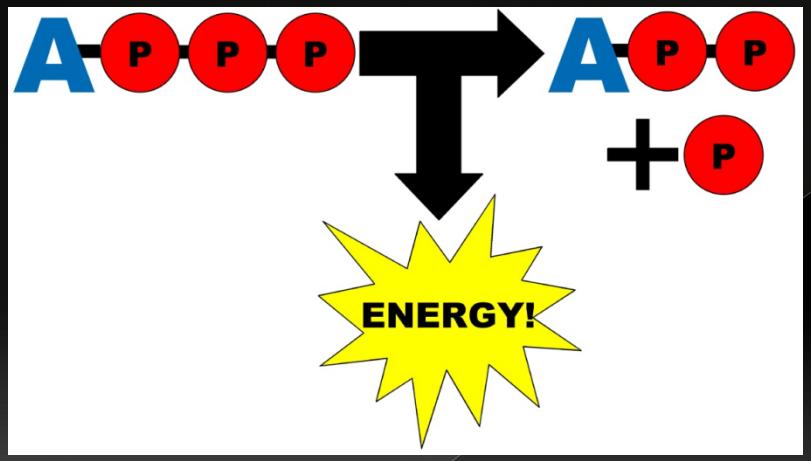


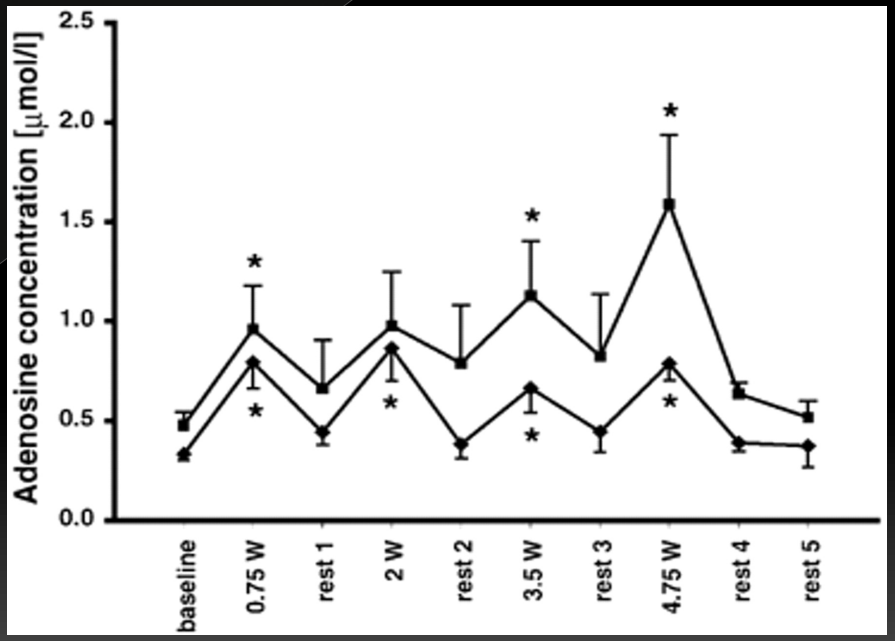


Green S et al. J Physiol 2000;529:849-861

Proposed Sympatholytic Agents

3. Adenosine

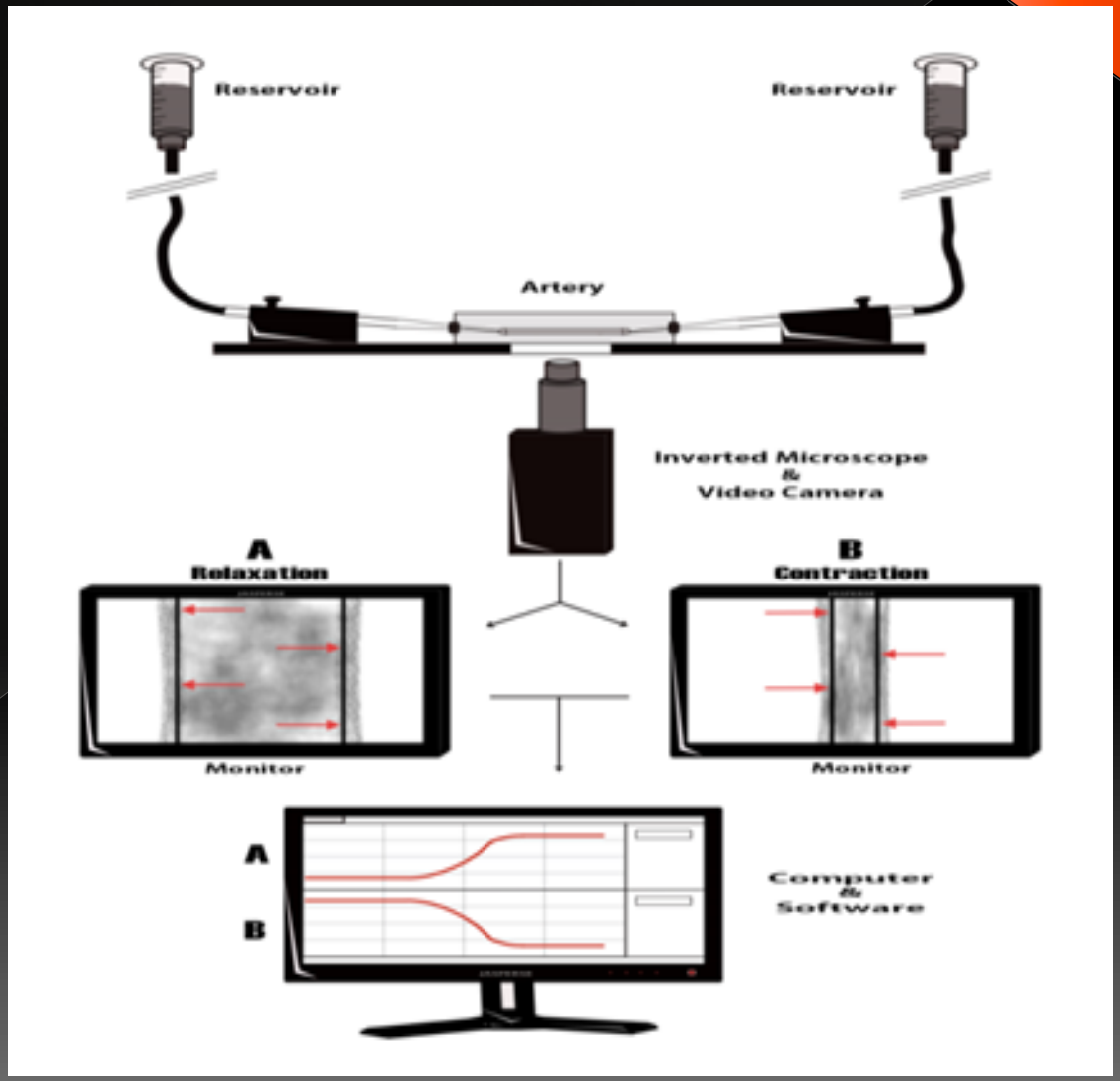




Langberg H et al. J Physiol 2002;542:977-983

The Set-Up

- Rat
  - -Anesthetized
- Artery
  - - Isolated
  - - Cannulated



Hypothesis

- Shear stress, potassium, and adenosine will cause a reduced α-1 mediated constriction.

Data Analysis

- Repeated Measures ANOVA
- Student's T-Test

RESULTS

Shear Stress

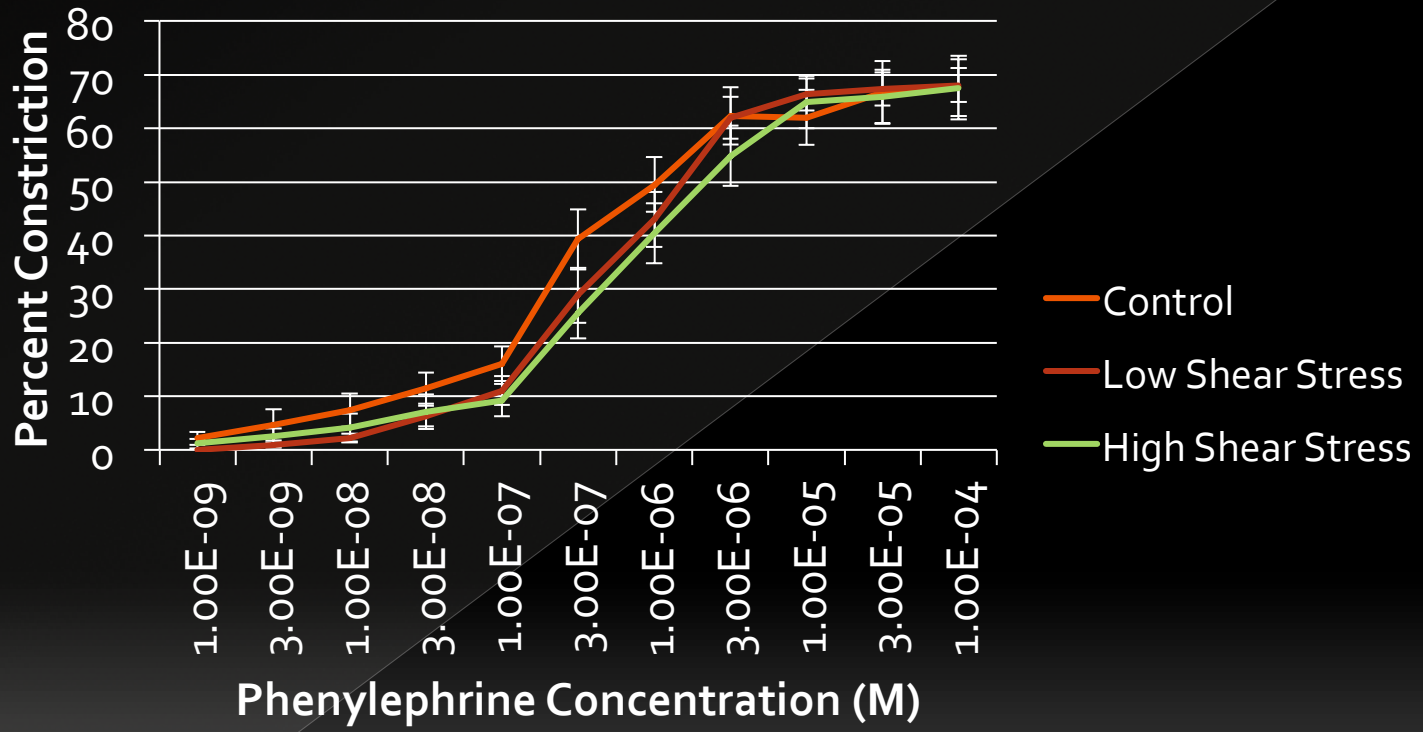


Figure 1: Shear Stress did not reduce constriction to Phenylephrine. Estimated shear stress values of 0 dy/cm², 25 dy/cm², and 135 dy/cm² were calculated for no, low, and high levels of shear stress, respectively (3). (N= 12 arteries from 12 rats)

Potassium

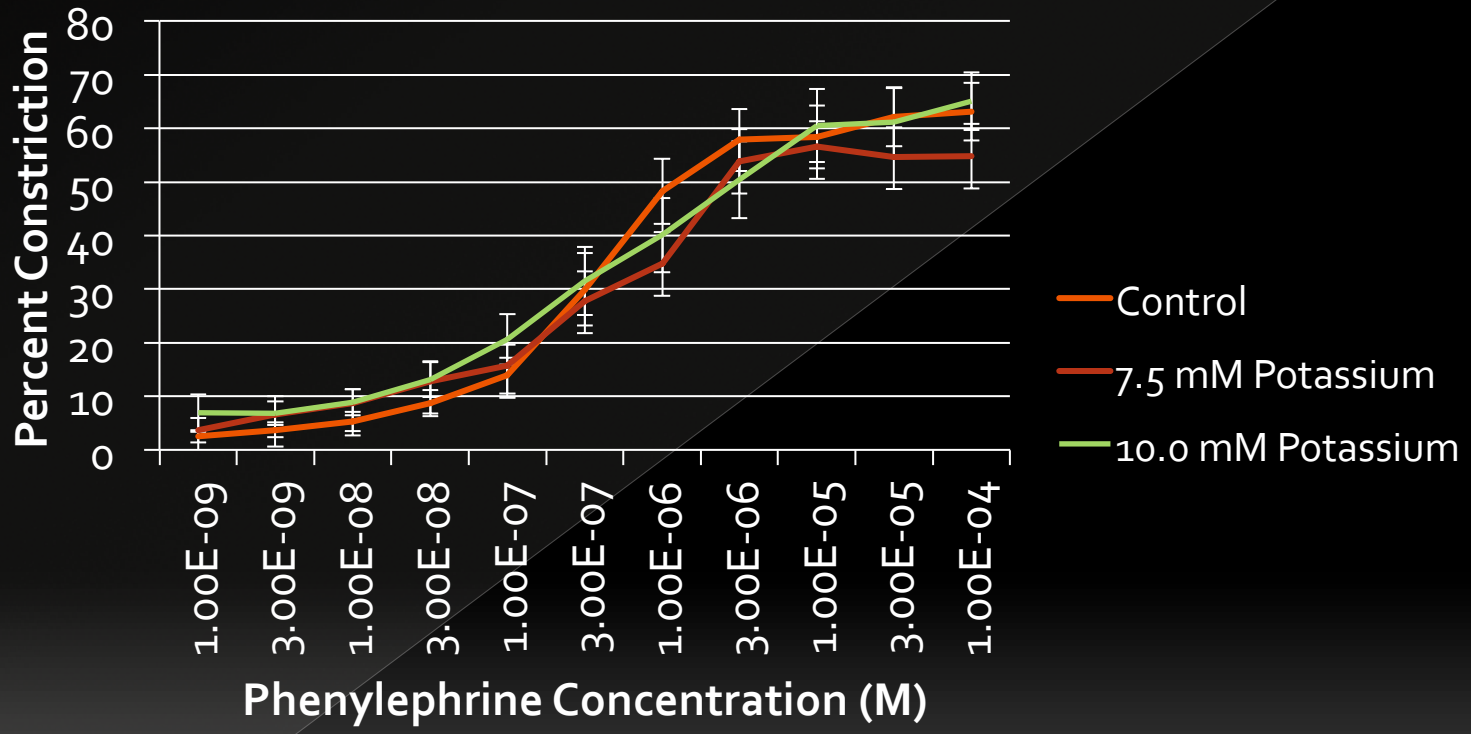


Figure 2: Potassium did not reduce constriction to Phenylephrine. Potassium concentrations of 5 mM, 7.5 mM, and 10 mM represent in vivo concentrations at rest, low-intensity exercise, and high-intensity exercise, respectively (6). (N= 17 arteries from 12 rats)

Adenosine

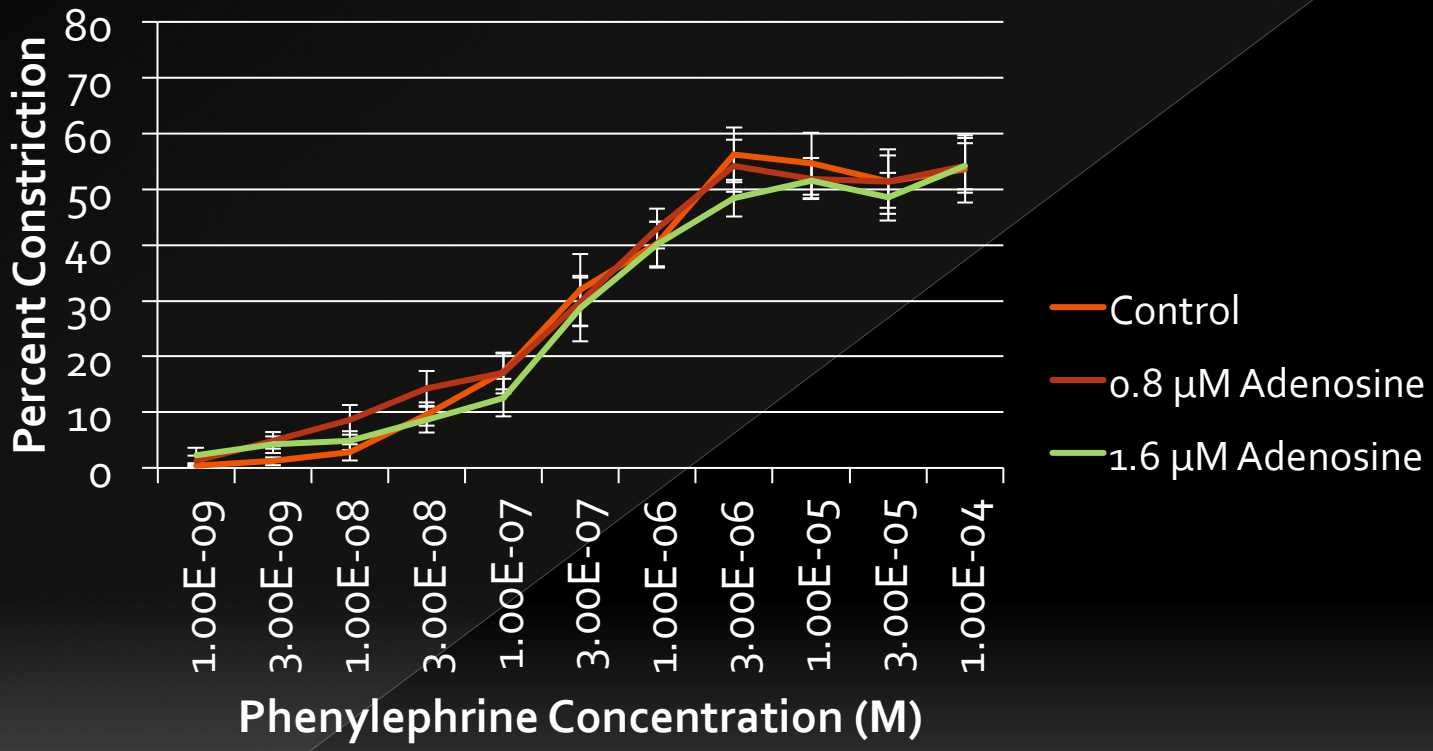


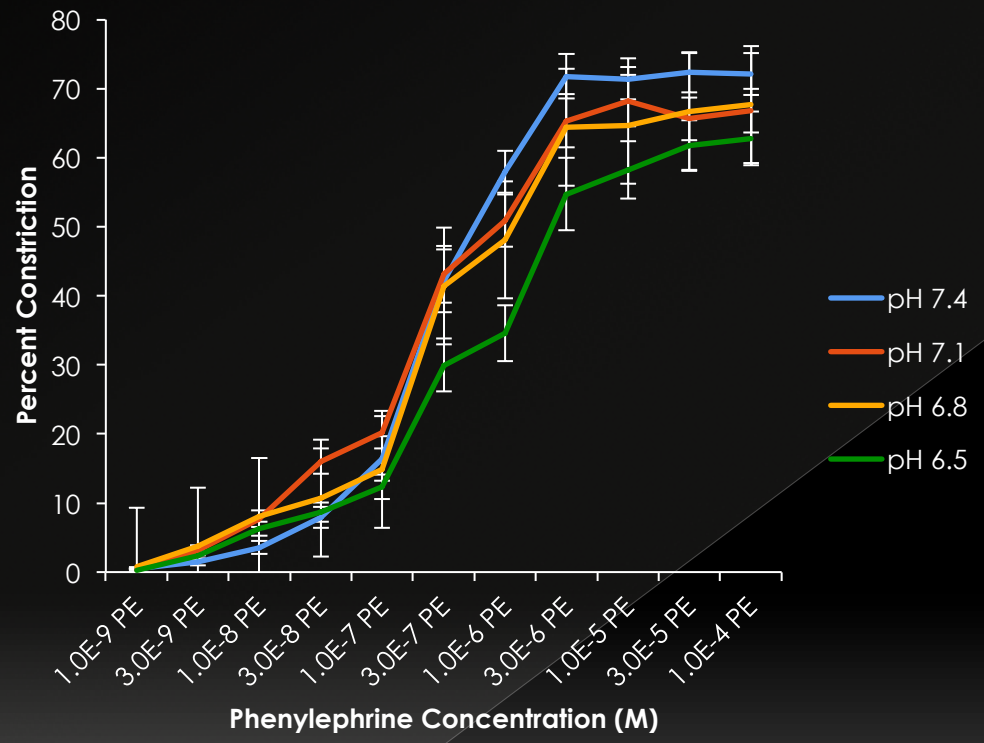
Figure 3: Adenosine (in vivo concentrations) did not reduce constriction to Phenylephrine. Adenosine concentrations of 0 µM, 0.8 µM, and 1.6 µM represent in vivo concentrations at rest, low-intensity exercise, and high-intensity exercise, respectively (7). (N= 12 arteries from 12 rats)

What's next?

- Not consistent with Ives et al.
  - Increased acidity is sympatholytic in alpha-1 receptors

- Consistent with Thomas et al.
  - Slow-twitch muscle (e.g. soleus) is not sensitive to sympatholysis

Acidosis Study



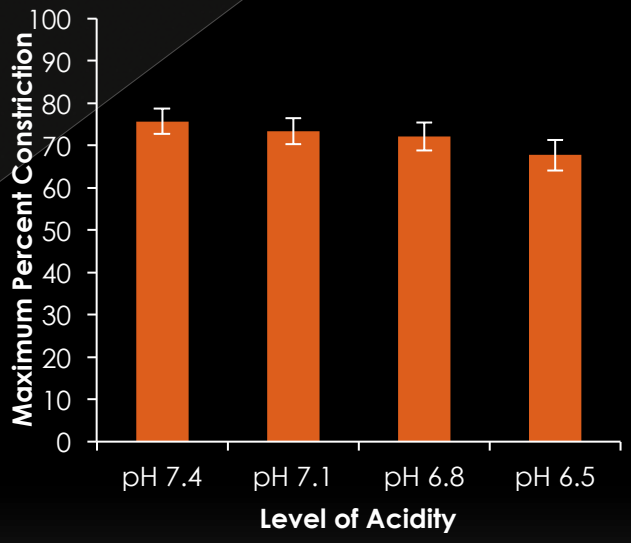


Figure 5: Increased acidity reduces vasoconstriction.
This line graph shows percent constriction curves of all four acidic solutions tested. (n = 22 rats)

Figure 6: Increased acidity reduces vasoconstriction.
This bar graph shows the maximum constriction value of all four acidic solutions tested. (n = 22 rats)

Acidosis Study

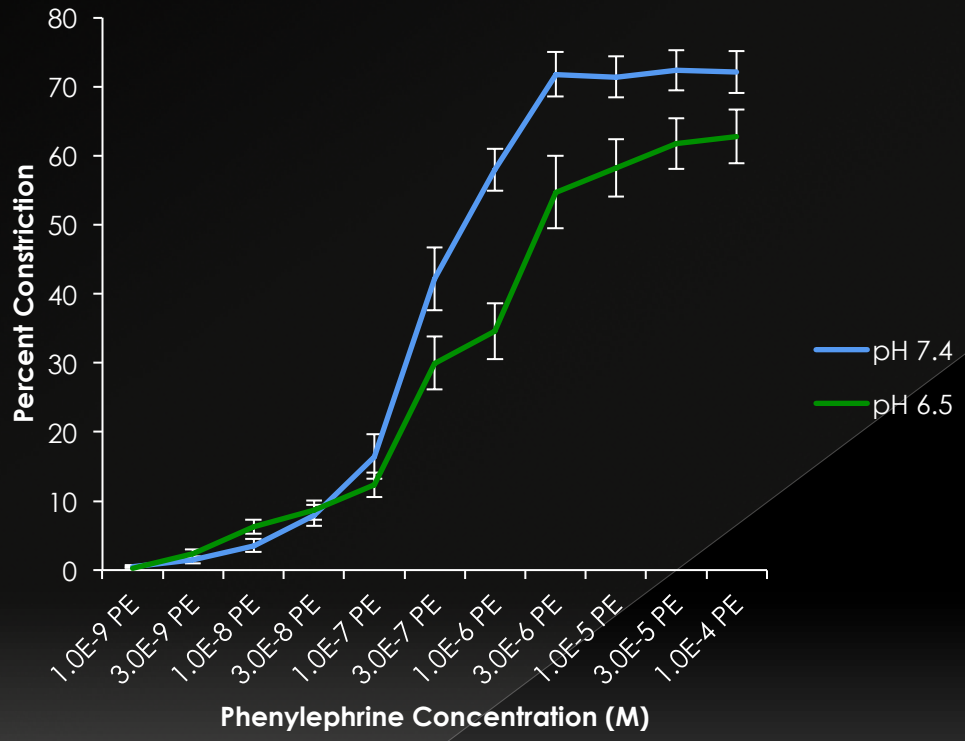


Figure 7: Increased acidity reduces vasoconstriction. This line graph shows percent constriction curves of the two significantly different solutions. (n = 22 rats)

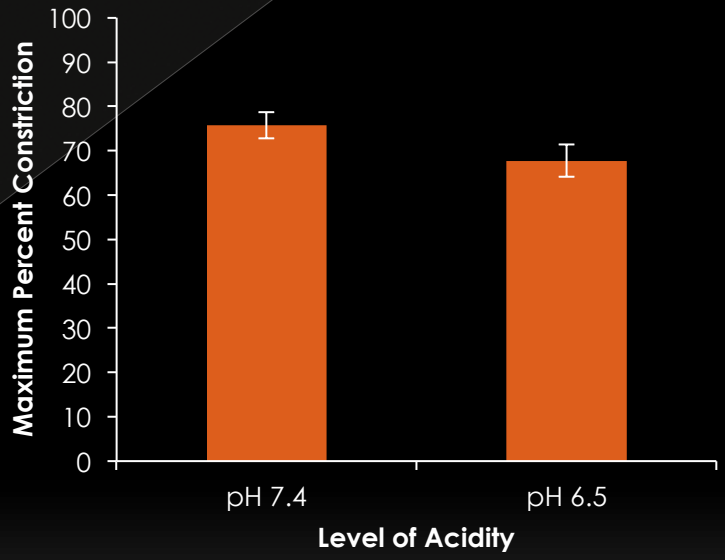


Figure 8: Increased acidity reduces vasoconstriction. This bar graph shows the maximum constriction value of the two significantly different solutions. (n = 22 rats)

Conclusions

- Shear stress, potassium, and adenosine are not sympatholytic in soleus feed arteries.
- Acidosis is mildly sympatholytic in soleus feed arteries.

Future

If soleus muscle arteries are sensitive to sympatholysis, do redundant mechanisms exist?

References

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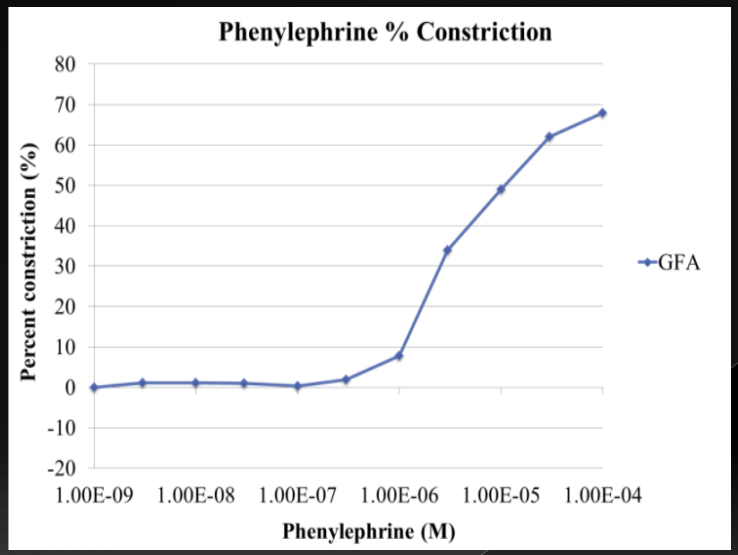
Dose-Response Curves



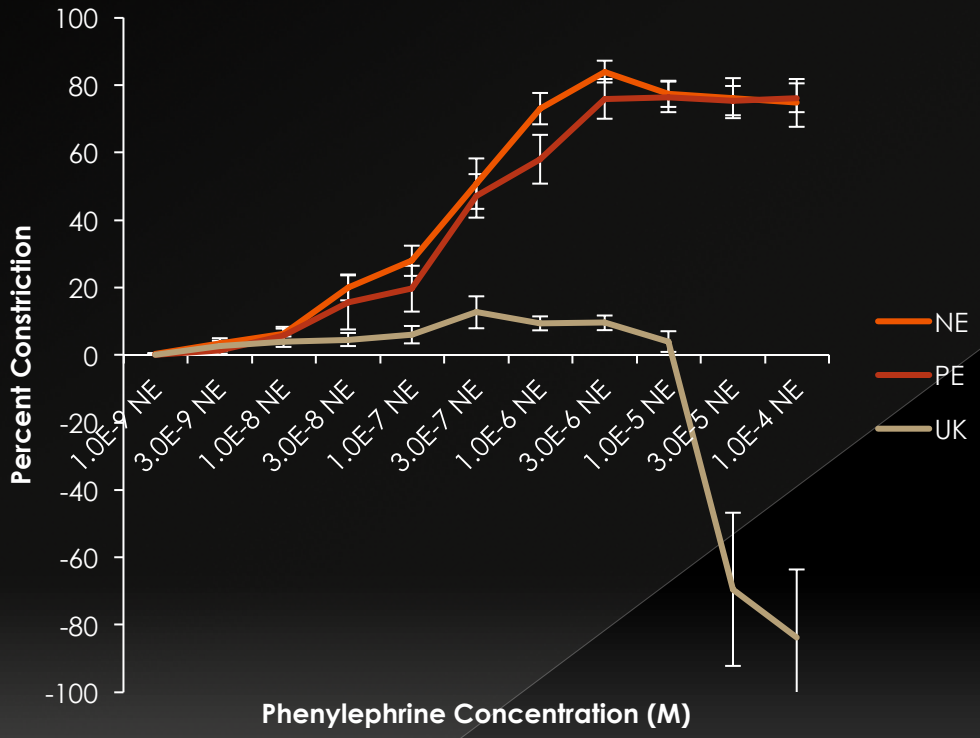
Conditions

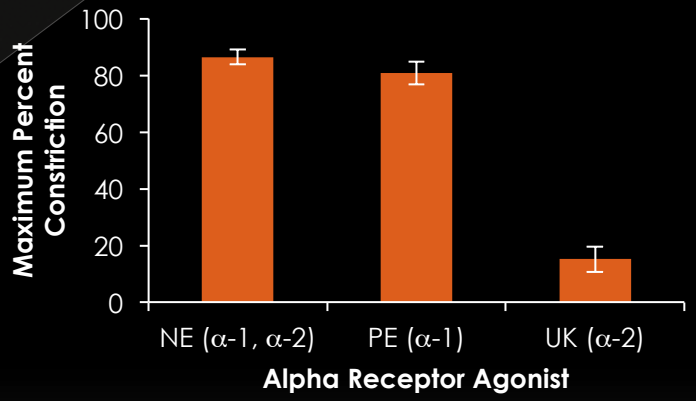
1. Shear Stress
   Control: PE + No Flow
   Treatment: PE + Low Shear Stress (25 dy/cm^2)
   PE+ High Shear Stress (135 dy/cm^2)

2. Potassium (No Flow)
   Control: PE + 5.0 Mm K
   Treatment: PE + 7..5 mM K+
   PE + 10.0 mM K+

3. Adenosine (No Flow)
   Control: PE + 0 uM ADO
   Treatment: PE + 0.8 uM ADO
   PE+ 1.6uM ADO

Control Data





Alpha-1 Receptors are the only receptors responded to sympathetic signaling in the soleus. . Sympathetic constriction (NE) is controlled only by the alpa-1 receptors (agonist = PE) and not the alpha-2 receptors (agonist = UK). (n = 7 rats)