Bradykinin B1 Receptor Antagonism Prevents Angiotensin II-Induced Erectile Dysfunction

Brittney McCormick
Laboratory of Taben Hale, PhD
Department of Basic Medical Sciences
Introduction

• Chronic AngII treatment in rats induces hypertension and erectile dysfunction.

• AngII and bradykinin are vasoactive factors with opposing actions: AngII promotes penile detumescence, and bradykinin, via the B2R, facilitates erection.
Introduction

• AngII increases bradykinin B1R expression in heart & aorta.

• B1R stimulation promotes pathological remodeling.

• However, the role of the B1R in erections and penile structure is unknown.

• The present study investigated the impact of B1R antagonism on AngII-induced erectile dysfunction.
Methods

• Sprague-Dawley rats (4wk treatment):
  – Vehicle
  – AngII (200ng/kg/min)
  – AngII + B1R antagonist R-954 (400 μg/kg/day)
  – R-954

• Mean arterial pressure (MAP) was measured via carotid artery cannulation.

• Erectile function was assessed via ICP/MAP following EFS of the cavernous nerve.
Methods

- The cross sectional area (CSA) of the coronary artery, aorta, penile dorsal artery were measured.

- Collagen content in the corpora cavernosa, & LV were measured via hydroxyproline assay.

- eNOS, Akt, and p38 in corpora cavernosa were assessed by western blotting.
AngII significantly increased mean arterial pressure and left ventricular mass. Left ventricular hypertrophy was prevented by B1R antagonism.
Concomitant B1R antagonism prevented AngII-induced erectile dysfunction

2-way ANOVA: significant main effects for Treatment and Voltage
Tissue-Specific Effect of AngII and B1R Antagonist Treatment

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- †: Are means signif. different? (P < 0.05)

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AngII significantly increased left ventricular collagen content. This effect was partially attenuated by concomitant B1R antagonism.
No significant difference in cavernosal collagen content was observed between treatment groups.
No significant difference in cavernosal eNOS expression was found.
No significant difference in cavernosal p38 or Akt expression was found.
Summary

• In Sprague Dawley rats, AngII produced the following changes:
  • Induced erectile dysfunction
  • ↑ MAP
  • ↑ Left ventricular mass
  • ↑ Coronary artery CSA
  • ↑ Aortic CSA
  • ↑ Left ventricular collagen content

• B1R antagonism attenuated these effects in all cases except MAP and aortic remodeling.
Neither AngII nor B1R antagonism produced significant changes in the following:

- Dorsal artery CSA
- Cavernosal collagen content
- ROS (not shown)
- Expression of eNOS, Akt, and p38 in corpora cavernosa
Perspectives

• AngII induces mitogenic and fibrogenic responses in the left ventricle and aorta, but not in erectile tissue.

• This study demonstrates that B1R blockade can offset AngII-induced ED independent of hypertension and cavernosal fibrosis.
Future studies will determine the mechanism underlying the unique response to AngII and B1R antagonism in the corpora cavernosa and provide further insight into the interaction between the renin angiotensin and kallikrein kinin systems in erectile tissue.
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The cross sectional area of the coronary artery and aorta significantly increased in response to AngII.