Mid Atlantic Regional Chapter
of the
American College of Sports Medicine

Annual Scientific Meeting, November 5th- 6th, 2021
Conference Proceedings
International Journal of Exercise Science, Issue 9, Volume 10

Estrogen Augments the Cardiac Functional Response to β2-Adrenergic Receptor Stimulation in Young Female Rat Hearts

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Sexual dimorphism exists throughout the cardiovascular system and is likely to play a role in the lower risk of hypertension, heart failure, and cardiovascular disease in pre-menopausal women compared to age-matched men. Alterations in β-adrenergic receptor (β-AR) signaling have been implicated in the development of heart failure, with aging associated with blunted cardiac β-adrenergic responsiveness. Previous studies report blunted increases in heart rate and contractility upon β-AR stimulation in female compared to male hearts. **PUPOSE:** Therefore, the purpose of this study is to evaluate the role of estrogen on the responsiveness of male and female rat hearts to β2-adrenergic stimulation. **METHODS:** Young (<8 months) and aging (>20 months) male and female rats were anesthetized, hearts were excised, and Langendorff-perfused. First, in young male and female rat hearts, dose-response curves were generated for either 17-β-estradiol or the β2-AR agonist, albuterol. Then, the estradiol dose which consistently resulted in maximal vasodilation was used to evaluate the interaction between estrogen receptor and β2-adrenergic receptor signaling. 20 uM 17-β-estradiol was added to the perfusate, and after steady state function was established in the presence of estrogen, dose-response curves for albuterol were again generated in young and aging rats. **RESULTS:** Increases in heart rate upon addition of albuterol were blunted in young female compared to young male rat hearts (from 244 ± 12 to 298 ± 11 beats/min in males, and from 236 ± 10 to 252 ± 25 beats/min in females). When estrodial was added to the perfusate prior to albuterol, functional responses were rescued in the young female rat hearts (from 225 ± 8 to 278 ± 8 beats/min in males, and from 225 ± 9 to 271 ± 10 beats/min in females). Aging male and females demonstrated similar increases in HR in response to albuterol (from 207 ± 8 to 253 ± 5 beats/min in males, and from 210 ± 9 to 267 ± 6 beats/min in females). **CONCLUSION:** Cardiac responses to β-adrenergic stimulation were blunted in young female compared to young male hearts; however, the presence of estrogen rescued the response such that it matched that of male hearts. The findings in this study indicate that the presence of estrogen may play an important role in stimulation of cardiac function via β-AR signaling in female hearts.