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Cardiac Response to β2-Adrenergic Stimulation is Attenuated in Old Rats Despite Higher Protein Expression

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Age and biological sex affect the heart's response to β-adrenergic receptor (β-AR) stimulation. Cardiomyocytes from young females have a lower contractile response to β-AR stimulation than young males, and increasing age is associated with blunted increases in heart rate and contractility upon β-AR stimulation. This may be due to the altered β-AR density, altered pathway signaling, or both. **Purpose:** Therefore, the purpose of this study is to evaluate the effect of age on β2-adrenergic receptor (β2-AR) protein expression and cardiac responsiveness to β2-adrenergic stimulation in male and female rat hearts. **Methods:** Young (<8 months), middle-aged (10 months) and old (>20 months) male and female rats were anesthetized, hearts were excised, and Langendorff-perfused. Dose response curves were generated utilizing albuterol, a β2-AR agonist, in all groups, while heart rate, coronary flow rate, and oxygen consumption were continually monitored. Heart samples were saved and homogenized to evaluate the β2-AR expression via western blot. **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 male hearts, and from 236 ± 10 to 252 ± 25 beats/min in female hearts). Middle-aged rats showed similar increases in heart rate (males: 221 ± 15 to 272 ± 20 beats/min, females: 226 ± 9 to 296 ± 47 beats/min). Old male and females demonstrated similar increases in heart rate that were blunted compared to middle-aged rats (males: 195 ± 7 to 235 ± 7 beats/min, females: 225 ± 35 to 240 ± 0 beats/min). Despite this, β2-AR expression was higher in old rat hearts compared to young rats. **Conclusion:** Cardiac responses to β-adrenergic stimulation were blunted in young female compared to young male hearts; however, the age effects eliminate the sex difference in β2-AR stimulation response. The findings in this study indicate that impairment of the β2-AR signaling pathways may play a role in the decreased responsiveness in old rat hearts, as β2-AR protein expression was higher in old compared to young rats.