论著

异丙肾上腺素致大鼠心肌肥厚时心肌细胞核Ca²⁺转运 ^{王培勇1*}, 刘 健², 许蜀闽¹, 唐朝枢³

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摘要 目的 观察异丙肾上腺素 (Iso) 致大鼠心肌肥厚模型心肌细胞核 45 Ca $^{2+}$ 摄取、钙释放通道肌醇1,4,5-三磷酸 (IP $_3$) 受体 (IP $_3$ R) 和ryanodine 受体 (RyR) 的动力学变化,以探讨细胞核Ca $^{2+}$ 的转运是否参与心肌肥厚发生。方法 Iso (sc 20、10和5 mg • kg $^{-1}$ 剂量递减3 d,3 mg • kg $^{-1}$ 维持7 d) 制备大鼠心肌肥厚模型,用差速离心和蔗糖密度梯度离心提纯心肌细胞核,用 45 Ca $^{2+}$ 同位素法测定细胞核钙摄取,用 [3 H] 标记配体分析心肌细胞核IP $_3$ R和RyR的动力学特点。结果 与对照组相比,Iso可导致大鼠心肌显著肥大,伴有显著心肌纤维化;心肌细胞核膜IP $_3$ R与其配体的最大结合容量 (B $_{\max}$)减少23. 4% (2 Co.05),解离常数 (2 Co.01),最大摄取与对照组相比降低 62% (2 Co.01),战半数最大摄取时 [Ca $^{2+}$] 无显著变化。结论 Iso导致大鼠心肌肥厚纤维化发生过程中,心肌细胞核 45 Ca $^{2+}$ 摄取能力降低,核上RyR数目上调,而IP $_3$ R数目下调,受体亲和力无变化,提示心肌细胞核钙调节系统参与心肌肥厚的发生过程。

 关键词
 肌肥厚
 细胞核
 受体, 肌醇1,4,5
 三磷酸
 受体, ryanodine
 钙
 异丙肾上腺素

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Nuclear Ca²⁺ transport of isoprenaline-induced heart hypertrophy in rats

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Abstract

AIM To investigate whether rat's myocardial nuclear Ca²⁺ transport system is involved in the isoprenaline (Iso)-induced cardiac hypertrophy. **METHODS** The model of rat myocardial fibrosis and hypertrophy was established by subcutaneous injections of Iso (20, 10 and 5 mg·kg⁻¹·d⁻¹ for 3 d, subsequently 3 mg·kg⁻¹·d⁻¹ for 7 d). Velocity and sucrose isopyknic gradient centrifugation were employed to fractionate rat cardiac nuclei. Myocardial nuclear calcium uptake was assayed with ⁴⁵Ca

 $^{2+}$ isotope. The maximal binding (B_{max}) and affinity (K_d) of IP₃ and ryanodine to their nuclear receptors were measured by

[3 H] ligand binding assay. **RESULTS** Iso increased the blood pressure and the cardiac hypertrophy. B_{max} of IP₃ binding to its receptors in cardiac nuclear envelopes decreased by 23.4% (P<0.05), and B_{max} of ryanodine binding to its receptors increased by 59.9% (P<0.01), Both K_d of IP₃ and ryanodine binding to their receptors were not changed (P>0.05) in hypertrophic myocardium as compared with control. Significant decrease in nuclear 45 Ca²⁺ uptake was observed and the maximal uptake was lowered by 62% as compared with that of control (P<0.01), but the half maximal [Ca²⁺] uptake remained unchanged. **CONCLUSION** These results indicate that the changes of nuclear Ca²⁺ transport system in myocardial nuclei may be involved in the Iso-induced myocardial hypertrophy.

Key words heart hypertrophy cell nucleus receptors inositol 1 4 5-triphosphate receptors ryanodine calcium isoprenaline

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