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Both $^{45}Ca^{2+}$ Uptake and $^{45}Ca^{2+}$ Release were Decreased in the Junctional Sarcoplasmic Reticulum Vesicles of Diabetic Heart

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Abnormally high Ca^{2+} concentrations have been reported in the cardiac myocytes of diabetic mellitus (DM). In order to elucidate the molecular mechanisms of the intracellular Ca^{2+} overload, the activities of $^{45}Ca^{2+}$ uptake and $^{45}Ca^{2+}$ release were measured from the vesicles of junctional SR (Heavy SR, HSR). Streptozotosin-induced diabetic rats were prepared and HSR vesicles were isolated from the ventricular myocytes. The pattern of SR $^{45}Ca^{2+}$ uptake in various preparations are following; the uptake was 6.7 pmol/μg protein in the HSR vesicles of control heart, 3.9 pmol/μg protein in DM heart, and 4.8 pmol/μg protein in the insulin-treated DM heart. SR $^{45}Ca^{2+}$ uptake matched with the activity of SR Ca^{2+}-ATPase. The activity of SR Ca^{2+}-ATPase was 562$\pm$7 nmol/min/mg protein in the HSR vesicles of control rat. The activity decreased to 353$\pm$8 (~60% of control) in the DM heart and it was recovered to 427$\pm$16 (~75% of control) in the insulin-treated DM heart. A similar pattern of $^{45}Ca^{2+}$ release in the presence of thapsigargin, a specific antagonist of SR Ca^{2+}-ATPase, was also observed. The highest release of 45% was observed in the HSR vesicles of the control heart. The release in the DM heart was 23.8% and it was 28.1% in the insulin-treated DM heart. In conclusion, the activities of both SR Ca^{2+}-ATPase and SR Ca^{2+} release channel (ryanodine receptor) were decreased in the diabetic cardiomyopathy.