Abnormal Platelet Ca^{2+} Handling in SHR and Stroke-Prone SHR evoked by Thromboxane A2 analog (U46619)—Comparison with Thrombin-Stimulation—.
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We have previously reported that the cytosolic free Ca^{2+} concentration ($[\text{Ca}^{2+}]_i$) is increased in platelets from spontaneously hypertensive rats (SHR) both in basal and thrombin-stimulated conditions compared to Wistar-Kyoto (WKY) rats. The purpose of this study was to confirm the correlation between elevated blood pressure and enhanced cellular Ca^{2+} handling by using thromboxane A2 analog (U46619) and thrombin.

We determined basal and agonist evoked $[\text{Ca}^{2+}]_i$ rise in fura-2-loaded platelets of male 12-13 weeks of age SHR, SHRSP, and WKY ($n=10$; respectively). Thrombin (0.1 units/mL) and U46619 (1 $\mu\text{mol/L}$) were used as agonists. We also evaluated the $[\text{Ca}^{2+}]_i$ response to 5 $\mu\text{mol/L}$ ionomycin in Ca^{2+} free buffer, as an index of the intracellular Ca^{2+} discharge capacity.

Systolic blood pressure was in the descending order of SHRSP>SHR>WKY (211 ± 8 , 173 ± 8 and 138 ± 4 mm Hg, respectively). Basal $[\text{Ca}^{2+}]_i$ was significantly higher in SHR than in WKY (44.3 ± 3.2 vs. 40.7 ± 3.5 nmol/L, $p<0.05$), whereas that in SHRSP (39.7 ± 3.2 nmol/L) was similar to WKY. Thrombin-stimulated $[\text{Ca}^{2+}]_i$ rise was greater in SHR than in WKY in the presence (496 ± 56 vs. 437 ± 352 nmol/L, $p<0.05$) and absence (264 ± 27 vs. 248 ± 25 nmol/L, $p<0.05$) of extracellular Ca^{2+} . But it was smaller in SHRSP than in WKY (395 ± 25 vs. 437 ± 52 nmol/L, $p<0.05$) in the presence of extracellular Ca^{2+} . On the contrary, U46619-stimulated $[\text{Ca}^{2+}]_i$ rise was smaller in SHR and SHRSP than in WKY in the presence (185 ± 23 and 136 ± 28 vs. 236 ± 36 nmol/L, $p<0.05$) and absence (101 ± 16 and 106 ± 14 vs. 141 ± 16 nmol/L, $p<0.05$) of extracellular Ca^{2+} . The intracellular ionomycin-released calcium fraction was similar in WKY, SHR and SHRSP (752 ± 112 , 716 ± 63 and 702 ± 67 nmol/L, respectively).

In SHR, thrombin-stimulated intracellular Ca^{2+} metabolism was enhanced but it was attenuated when stimulated by U46619. In contrast to SHR, in SHRSP, both thrombin and U46619-stimulated $[\text{Ca}^{2+}]_i$ rise was attenuated. These results suggest that $[\text{Ca}^{2+}]_i$ increasing mechanism is not always functioning greater in SHR than in WKY. Furthermore, platelet Ca^{2+} handling differs between different SHR substrains, and an increased $[\text{Ca}^{2+}]_i$ is not an obligatory phenomenon in genetically hypertensive rats.