The mechanism of serotonin-induced increase in intracellular Ca^{2+} and constriction via Rho kinase in rat thoracic aortas

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The mechanism of serotonin (5-HT)-induced vasoconstriction and intracellular Ca^{2+} ($[Ca^{2+}]i$) mobilization is not completely elucidated. 5-HT-induced vasoconstriction partly involves Ca^{2+}-independent activation of Rho kinase. However, the mechanism of Rho kinase activation by 5-HT is still unknown. We examined the mechanism of 5-HT-induced $[Ca^{2+}]i$ mobilization of rat aortic smooth muscle cells using microscopic fluorometry. We also investigated whether 5-HT-induced constriction in rat thoracic aortas is mediated by Rho kinase activation through Src, epidermal growth factor receptor (EGFR), and extracellular signal-regulated kinase (Erk).

5-HT induced a biphasic $[Ca^{2+}]i$ response, and the initial $[Ca^{2+}]i$ increase was attenuated by inositol triphosphate (IP_3) receptor blocker, and inhibitors of Src and phosphoinositide 3-kinase (PI3K), but not L-type Ca^{2+} channel blocker (LCBB). The second $[Ca^{2+}]i$ increase was attenuated by LCBB. Contractile response to 5-HT significantly attenuated by inhibitors of Rho kinase, Erk1/2, Src, and EGFR. These data suggest that 5-HT induces Ca^{2+} release from the endoplasmic reticulum via Src and PI3K, and subsequently extracellular Ca^{2+} influx via L-type Ca^{2+} channel, and 5-HT-induced constriction is mediated by Rho kinase activation via Src, EGFR, and Erk in rat thoracic aortas.