選擇性血清素轉運體抑制劑能抑制人類血小板被蛇毒蛋白 convulxin 與纖維蛋白原所刺激的 Syk 磷酸化

Selective Serotonin Reuptake Inhibitors Inhibit Convulxin- and Fibrinogen-Induced Phosphorylation of Syk in Human Platelets

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目的(Objective)：Background: Selective serotonin reuptake inhibitors (SSRIs) have been reported to reduce platelet aggregation induced by collagen and convulxin. Collagen and convulxin induce platelet aggregation through glycoprotein VI (GPVI)-FcR γ -ITAM-Syk signaling pathway. In addition, binding of fibrinogen to platelets triggers the FcγRII-ITAM-Syk signaling pathway. Objectives: To characterize the inhibitory properties of SSRIs on GPVI-mediated platelet aggregation and to investigate the effects of SSRIs on GPVI-FcR γ -ITAM-Syk signaling pathway. The effect of SSRIs on fibrinogen-induced Syk phosphorylation was also investigated.
方法(Methods)：Methods: Citalopram, a relatively pure SSRI, was used in this study. Platelet aggregation was measured by aggregometry. The influence of acute treatment of citalopram on platelet serotonin was determined. Fibrinogen adhesion assay was used to examine the effect of citalopram on fibrinogen-induced Syk phosphorylation. Signaling pathways were evaluated by immunoprecipitation and Western blotting.
結果(Results)：Results: Citalopram concentration-dependently inhibited convulxin-induced platelet aggregation. Citalopram inhibited the release of serotonin in response to convulxin. Serotonin concentration in washed platelets, however, was unchanged after acute treatment of citalopram. Citalopram did not influence the effect of serotonin on platelets. Convulxin-induced phosphorylations of Syk, LAT, PKCδ and Akt were inhibited by citalopram. Although citalopram inhibited the interaction between FcRγ and Syk , the phosphorylation of FcRγ in response to convulxin remained unchanged. Furthermore, citalopram inhibited the increase of the interaction between serotonin transporter (SERT) and Syk induced by convulxin. In addition, citalopram inhibited the adhesion of platelets to immobilized fibrinogen and fibrinogen-induced SyK phosphorylation.
討論(Conclusion)：Conclusions: SSRIs inhibit convulxin- and fibrinogen-induced Syk phosphorylation. They influence the interaction between GPVI-FcR γ -ITAM and SyK.