

Liver blood flow is regulated by hepatic stellate cells and sympathetic nerve in the sinusoid

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The diameter of sinusoid has been shown to be changed by perfusion of adrenaline and acetylcholine. Thus, the liver blood flow is suggested to be regulated by the autonomic nervous systems in the sinusoid. However, it remains to be elucidated which cells in the sinusoid are involved in the response. The present study focused on hepatic stellate cells (HSCs) encircling the sinusoid and aimed to determine 1) whether HSCs constrict in response to noradrenaline (NAd) and 2) whether HSCs regulate liver blood flow. To measure HSC constriction quantitatively, we developed a novel method using fluorescent beads. We observed that HSCs constricted in response to NAd, which was suppressed by the α_1 -adrenoceptor inhibitor bunazosin and the non-muscle myosin II inhibitor blebbistatin (Bleb; 1 μ M). In contrast, Bleb (1 μ M) had no effect on the contraction of isolated portal veins. The NAd-induced constriction of HSCs was also suppressed by xestospongins C, YM-58483, W-7, ML-9, and H-1152. In addition, Bleb (1 μ M) decreased the perfusion pressure of the liver increased by NAd. This response appears to be due to HSC relaxation, since Bleb had the inhibitory effect on HSCs but not on portal veins. These results suggest that NAd induces constriction of HSCs via increasing Ca^{2+} influx and Ca^{2+} sensitization, thereby regulating liver blood flow.