Role of N-methyl-D-aspartate receptors in gastric mucosal blood flow induced by histamine

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摘要

Abstract

Ionotropic N-methyl-D-aspartate (NMDA) receptor agonists, L-aspartic acid (L-Asp) and NMDA, have been shown to inhibit histamine-stimulated acid secretion, but their effect on gastric mucosal blood flow (GMBF) is largely unknown. The aim of this study was to investigate whether L-Asp and NMDA inhibit histamine-stimulated GMBF and to examine the expression patterns of NMDA receptor subunits NR1, NR2A, and NR2B in rat stomach. Laser Doppler flowmetry was used to measure gastric blood flow in anesthetized rats. The GMBF was assessed during an intravenous infusion of histamine in the presence of tripelennamine. The effects of L-Asp and NMDA on histamine-induced gastric blood flow were examined. In addition, the distribution patterns of NR1-, NR2A-, and NR2B-contaning NMDA receptors in rat stomach were determined immunohistochemically by using specific antibodies against NR1, NR2A, and NR2B. Histamine-induced enhancement of GMBF depended on acid secretion and the activation of H(2)-receptors. Neither L-Asp nor NMDA had an effect on the spontaneous GMBF. However, L-Asp and NMDA reduced the histamine-induced increase in GMBF. DL-2-amino-5-phosphonopentanoic acid (AP-5), an NMDA receptor antagonist; and prazosin, an alpha(1)-receptor antagonist; but not propanolol, a beta(2)-receptor antagonist; or yohimbine, a alpha(2)-receptor antagonist; reversed the inhibitory effect of L-Asp and NMDA on the histamine-induced increase in GMBF. Therefore, L-Asp and NMDA inhibit histamine-induced GMBF via a mechanism involving the activation of NMDA receptors and alpha(1)- adrenoceptors. The fact that NMDA receptor subunits NR1, NR2A, and NR2B were found to be localized in the rat stomach as visualized immunohistochemically with specific antibodies against NR1, NR2A, and NR2B is consistent with this hypothesis.