

# **Effect of excitatory amino acid neurotransmitters on acid secretion in the rat stomach**

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摘要

## **Abstract**

Excitatory amino acids (EAAs), in particular, L-aspartate (L-Asp) neurons and their processes, were localized in the rat stomach using an immunohistochemical method with specific antibodies against either L-Asp or its synthesizing enzyme, aspartate aminotransferase (AAT). Myenteric ganglia and nerve bundles in the circular muscle and in the longitudinal muscle were found to be AAT- or L-Asp-positive. In addition, AAT- or L-Asp-positive cells were also found in the muscle layer and the deep mucosal layer. The distribution of AAT- or L-Asp-positive cells in both the mucosal and muscle layers was heterogeneous in the stomach. In addition, L-Asp at  $10^{-6}$  M negligibly influenced acid secretion in an everted preparation of isolated rat stomach. However, according to our results, L-Asp markedly inhibited the histamine-stimulated acid secretion, but not the oxotremorine- or the pentagastrin-stimulated acid secretion. Furthermore, L-Asp also inhibited histamine-induced elevation of cAMP. L-Asp itself did not affect the cAMP level although it elevated the cGMP level in the stomach. Moreover, either (+)2-amino-5-phosphonovaleric acid or ( $\pm$ )3-(2-carboxypiperazin-4-yl)propyl-1-phosphonic acid, i.e. two specific antagonists for N-methyl-D-aspartic acid (NMDA) receptors, blocked the inhibitory effect of L-Asp on histamine-stimulated acid secretion or histamine-induced elevation of cAMP. Since cAMP has been strongly implicated as the second messenger involved in histamine-induced acid secretion, we believe that L-Asp regulates acid secretion in the stomach by inhibiting histamine release through the NMDA receptors, subsequently lowering the level of cAMP and ultimately reducing acid secretion.