

## 論 文 要 旨

〔 *Helicobacter pylori* が産生する外毒素 VacA は Ucn1-CRF 受容体軸  
を介して摂食を抑制し、不安様行動を惹起する 〕

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*Helicobacter pylori* (*Hp*) infection is related to the pathogenesis of chronic gastric disorders and extragastric diseases. Here, we examined the anorexigenic and anxiogenic effects of *Hp* vacuolating cytotoxin A (VacA) through activation of hypothalamic urocortin1 (Ucn1). VacA was detected in the hypothalamus after peripheral administration and increased Ucn1 mRNA expression and c-Fos-positive cells in the hypothalamus but not in the nucleus tractus solitarius. c-Fos and Ucn1-double positive cells were detected. CRF1 and CRF2 receptor antagonists suppressed VacA-induced anxiety and anorexia, respectively. VacA activated single paraventricular nucleus neurons and A7r5 cells; this activation was inhibited by phospholipase C (PLC) and protein kinase C (PKC) inhibitors. VacA causes anorexia and anxiety through the intracellular PLC-PKC pathway, migrates across the blood-brain barrier, and activates the Ucn1-CRF receptor axis.