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Ghrelin is an orexigenic signaling molecule with anxiogenic activity in discrete regions of the hypothalamus

Ghrelin, an endogenous ligand of the growth hormone secretagogue receptor (GHS-R), is a 28 amino acid acylated peptide recently identified in the rat stomach. Gene expression in the stomach is increased by tail pinch stress and by starvation. We have previously reported that injections of ghrelin into the arcuate and paraventricular nuclei stimulate eating and alter energy substrate utilization and energy expenditure. These effects are blocked by urocortin pretreatment. Recent evidence suggests that peripherally administered ghrelin significantly increases corticotropin releasing hormone (CRH) mRNA and increases serum corticosterone, while ventricular treatment induces anxiety-like behaviors in the rat. In the present study we assessed the orexigenic and anxiogenic action of ghrelin following microinjection into the arcuate nucleus (Arc), paraventricular nucleus (PVN), perifornical hypothalamus (PFH) and the ventromedial nucleus (VMN). To assess ghrelin's role in anxiogenic behavior, separate groups of rats were injected with vehicle, 50 pmol or 200 pmol and then placed in an elevated plus maze for 10 min. Each test was performed as a single trial per animal. Arc, PVN, PFH, and VMN ghrelin treatment significantly decreased the number of entries and time spent in the open arms of the maze. In separate testing, injection of the peptide into all hypothalamic areas significantly increased food intake over 2 h. These findings are consistent with the argument that ghrelin mediates neuroendocrine and behavioral responses to stress in addition to its role as a hypothalamic orexigenic peptide.