

Differential effects of intra-VTA ghrelin and glucagon-like peptide-1 on the stimulatory action of amphetamine and cocaine-induced alcohol intake

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Abstract

In order to further elucidate the role of mesolimbic peptides in the expression of alcohol reward, the present study investigated the effects of ghrelin and glucagon-like peptide-1 (GLP-1) on alcohol intake, in addition to alcohol intake stimulated by systemic d-amphetamine or cocaine treatment. All rats were initially habituated to a 6% alcohol solution. We then demonstrated that intraperitoneal injections of d-amphetamine and cocaine increased alcohol compared to the vehicle condition. In subsequent testing we examined the effects of ventral tegmental area (VTA) ghrelin or vehicle paired with a fixed dose of d-amphetamine or vehicle. In separate rats we then investigated the impact of the GLP-1 agonist exendin-4 (Ex-4), injected into the VTA, on alcohol intake alone, or when Ex-4 was co-administered with d-amphetamine or cocaine. Our results indicated that VTA ghrelin significantly increased alcohol intake, and most importantly, potentiated the effect of d-amphetamine and cocaine on alcohol consumption. Conversely, VTA Ex-4 inhibited alcohol intake and antagonized the stimulatory effect of d-amphetamine and cocaine on alcohol consumption. In a final study we further demonstrated that VTA Ex-4 treatment significantly inhibited the combined stimulatory effects of ghrelin paired with d-amphetamine or ghrelin paired with cocaine. Overall our findings are consistent with a critical role for both ghrelin and GLP-1 receptor mechanisms in mesolimbic alcohol reward circuitry. Moreover, our results further suggest that ghrelin and GLP-1 modulate the stimulatory effect of psychostimulants on alcohol intake.

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