Noradrenergic neurons of the area postrema mediate amylin's anorectic action

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Abstract

Peripheral amylin inhibits food intake via activation of the area postrema (AP). 59% of amylin-activated AP neurons are noradrenergic (NA), i.e., they express dopamine-beta-hydroxylase (DBH). Here, we wanted to test whether AP NA neurons mediate amylin's anorectic effect. We performed a specific lesion of AP NA neurons using a saporin conjugated to an antibody against DBH (DSAP). IgG-saporin was used in sham controls. After 2-3 weeks necessary for neuronal degeneration, we tested the rats for the effect of amylin (5 or 20 g/kg BW, s.c.) to reduce food intake. In a terminal experiment, the rats received amylin (20 g/kg) or saline; brain sections with the AP and nucleus of the solitary tract (NTS) were stained for DBH to assess lesion success and for c-Fos expression to evaluate amylin-induced neuronal activation. DBH staining revealed that 10 DSAP-injected rats had NA lesion equal to or above 50%, defined as successful; 6 had lesions below 50%. Daily food intake and body weight gain did not differ between lesioned and sham groups. Amylin-induced anorexia was observed in sham rats with both amylin doses, while rats with a successful lesion had no significant reduction in eating after either amylin dose. Rats with lesions below 50% only ate less after the higher amylin dose. In contrast to sham-lesioned animals, successfully NA-lesioned rats did not show amylin-induced c-Fos expression in the AP and NTS. These results provide first evidence for a functional role of NA neurons in the AP in the mediation of amylin's anorectic effect.
Noradrenergic neurons of the area postrema mediate amylin’s anorectic action

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Peripheral amylin inhibits food intake via activation of the area postrema (AP). 59% of amylin-activated AP neurons are noradrenergic (NA), i.e., they express dopamine-beta-hydroxylase (DBH). Here, we wanted to test whether AP NA neurons mediate amylin’s anorectic effect. We performed a specific lesion of AP NA neurons using a saporin conjugated to an antibody against DBH (DSAP). IgG-saporin was used in sham controls. After 2–3 weeks necessary for neuronal degeneration, we tested the rats for the effect of amylin (5 or 20 g/kg BW, s.c.) to reduce food intake. In a terminal experiment, the rats received amylin (20 g/kg) or saline; brain sections with the AP and nucleus of the solitary tract (NTS) were stained for DBH to assess lesion success and for c-Fos expression to evaluate amylin-induced neuronal activation. DBH staining revealed that 10 DSAP-injected rats had NA lesion equal to or above 50%, defined as successful; 6 had lesions below 50%. Daily food intake and body weight gain did not differ between lesioned and sham groups. Amylin-induced anorexia was observed in sham rats with both amylin doses, while rats with a successful lesion had no significant reduction in eating after either amylin dose. Rats with lesions below 50% only ate less after the higher amylin dose. In contrast to sham-lesioned animals, successfully NA-lesioned rats did not show amylin-induced c-Fos expression in the AP and NTS. These results provide first evidence for a functional role of NA neurons in the AP in the mediation of amylin’s anorectic effect.