Hindbrain noradrenergic input to paraventricular hypothalamus mediate the activation of oxytocinergic neurons induced by the satiety factor oleoylethanolamide

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Oleoylethanolamide (OEA) is a gut-derived lipid that stimulates vagal fibres to induce satiety. Our previous work has shown that peripheral OEA activates c-fos in the nucleus of solitary tract (NST) and in the paraventricular nucleus (PVN), where it enhances oxytocin (OXY) transmission. OEA anorexiant action can be prevented by the i.c.v. administration of a selective OXY receptor antagonist, suggesting a crucial role of OXY system in the pro-satiety effects of OEA. The NST is the source of a noradrenergic input to hypothalamic OXY neurons. We hypothesized that the activation of this pathway might mediate OEA effects on PVN neurons. Therefore we subjected rats to intra-PVN administration of the immunotoxin saporin (DSAP) that is targeted to destroy hindbrain noradrenergic neurons, and evaluated the effects of OEA (10 mg/kg i.p.) on feeding behavior, on c-fos expression in the PVN and OXY immunoreactivity in the PVN and neurohypophysis.
DSAP lesion prevented OEA effects on food intake, c-fos activation and OXY expression, while sham operated rats responded normally to OEA, showing a 70% decrease of food intake, a 3-fold increase of c-fos and OXY levels in the PVN and a 47% increase of pituitary OXY immunoreactivity. These findings support the hypothesis that noradrenergic NST-PVN projections are involved in the central release of OXY, which mediates OEA pro-satiety action and shed new light on the mechanism through which OEA controls satiety.