ABSTRACT

Obesity is an increasing health risk in modern society, correlating with multiple physiological and mental comorbidities such as type-2 diabetes and depression. AgRP neurons from the arcuate nucleus of the hypothalamus are key drivers of food intake feeding behavior. Their sustained effect on food intake was shown to relay on NPY release from their synapsis at their projection sides. One of these projection sides is the bed nucleus of the stria terminalis (BNST), a forebrain structure known for its involvement in stress and anxiety responses. Stimulation AgRP projections in the anterior BNST were shown to induce a profound food intake, exclusively in the presence of NPY.

In the present study, we identified a neuron population in the anterior-medial BNST (amBNST) expressing the NPY receptor 1 ($NPY1R^{amBNST}$), that is inhibited upon fasting. We show that this neuron populations mediates acute and prolonged food intake as well as anxiety-like behavior and locomotion. Further, we demonstrate its direct inhibitory input on dopaminergic neuron in the substantia nigra pars compacta, a crucial neuron population for locomotor activity. $NPY1R^{amBNST}$ neurons receive direct input from neurons of the ARC, a key nucleus for the regulation of food intake, and the CeA, an important brain region for processing anxiety and stress. We further show that GABAergic projections from the CeA into the amBNST strongly suppress food intake and increase locomotion in a hunger-state dependent manner, independent from $NPY1R^{amBNST}$ neurons.

The obtained data suggest that $NPY1R^{amBNST}$ neurons act as a relay between feeding and defensive behavior. Thus, $NPY1R^{amBNST}$ neurons and the demonstrated interconnections could serve as targets for novel approaches treating obesity and stress-related eating disorders on a neuronal base.