Twenty-four female rats were ovariectomized and received bilateral arcuate microinjections of either NK3-SAP or Blank-SAP (control). Three weeks later, animals were implanted with silastic capsules containing 17β-estradiol (E2) and 11 days after that, they were sacrificed. Body weights and blood samples were taken at the beginning of the experiment, three weeks after ovariectomy, and at 11 days after E2-treatment. Immunohistochemical studies revealed ablation of KNDy neurons by NK3-SAP. There was near-complete loss of NK3r neurons in the arcuate nucleus with a 94-98% reduction in the number of kisspeptin and neurokinin B neurons, compared to Blank-SAP rats (Figure 1). In contrast, proopiomelanocortin, neuropeptide Y and GnRH immunoreactive elements were preserved.

We found that ablation of KNDy neurons resulted in marked changes in LH secretion and the E2 modulation of body weight. In control animals, ovariectomy markedly increased serum LH and body weight and these effects were reversed by replacement with E2. In contrast, NK3-SAP-injected rats did not exhibit a significant rise in serum LH in response to ovariectomy, and serum LH was lower in these animals regardless of estrogen status (Figure 2A). Surprisingly, the effects of ovariectomy and E2 on body weight were blocked in rats with KNDy neuron ablation (Figure 2B). These data show an essential role of arcuate KNDy neurons for tonic LH secretion, the rise in LH in response to ovariectomy, and the E2 modulation of body weight.

References