**Supplementary Material**

**Supplement 1: Silencing GHSRlPBN cells does not alter food intake or body weight in mice fed a standard chow diet**

Here, we sought to determine the effect of silencing the GHSRlPBN cells on the evolution of food intake and body weight when mice are fed standard chow under the same period as for the mice fed the high-fat high-sugar diet (i.e. starting 1 week after surgery and for 23 days). Note that the timeline differs slightly from the mice fed a HFHS diet, since these animals continuously received chow, whereas the HFHS diet commenced one week after surgery.

**Materials and Methods**

Eleven heterozygous Ghsr-IRES-Cre (Ghsr-Cre Het) male mice and 9 wild-type male littermates (WT) were injected bilaterally into the lPBN with a viral vector (AAV1-CBA-DIO-eGFP-Tetox-WPRE-pA) (Carter et al., 2015) following an identical protocol to that stated in the “stereotaxic surgeries” section of the material and methods in the main text. The GHSRlPBN cells were, therefore, silenced in the Ghsr-Cre Het mice (now referred to as the GHSR-silenced group) but not in the WT controls. To investigate the effect of silencing GHSRlPBN cells on food intake and body weight when mice are given a standard chow diet, chow intake and body weight were measured 2-3 times a week, at the same time of the day (approximately at 12:00) for 23 days after surgery. In addition, caloric efficiency was calculated on Day 23 as follows: caloric efficiency = (body weight gain (g) / food intake (kcal)) x 100 (Rabasa et al., 2019). Five of the GHSR-silenced mice were excluded because post-mortem evaluation revealed that the injection site was off-target. One additional GHSR-silenced mouse was identified as an outlier by the SPSS software in the caloric efficiency data. Thus, the final analysis of body weight and food intake included 6 GHSR-silenced mice and 9 control mice and the analysis of caloric efficiency included 5 GHSR-silenced mice and 9 controls.

Data were analyzed using IBM SPSS Statistics 25 (IBM Corp., Armonk, NY, USA). All data were tested for normal distribution using a Shapiro-Wilk test and for homogeneity of variances using a Levene’s test. Throughout the 23 days of chow diet exposure, cumulative kcal intake and % body weight gain were analyzed by one-way repeated measures ANOVA with the measurement days as the within-subject factor. Caloric efficiency was analyzed using an independent samples Student’s t-test.

**Results**

The cumulative energy intake (kcal) from chow did not differ between GHSR-silenced and control mice (overall group effect on cumulative kcal intake: *F* (1, 13) = 0.00, *p* = 0.995) (Supp. Fig. 1A). Similarly, there was no difference in percentage body weight gain between the two groups over time (overall group effect on percentage body weight gain: *F* (1, 13) = 1.94, *p* = 0.187) (Supp. Fig. 1B). Finally, caloric efficiency was not affected in the GHSR-silenced mice (0.4 ± 0.5 g/kcal/day) compared to the controls (1.2 ± 0.8 g/kcal/day) (*t*(12) = 0.75, *p* = 0.470, Supp. Fig. 1A).



**Supplementary Figure 1.** **Effect of GHSRlPBN cells Tetox-silencing on chow intake and body weight. (A)** Cumulative chow intake in kcal over time and caloric efficiency (CE) on day 23 after surgery for the GHSR-silenced and the control groups **(B)** Evolution of % body weight gain of both groups on standard chow diet over time (body weight at 1 week after surgery = 100 %). Data shown as mean ± SEM.

**References**

Carter, M.E., Han, S., and Palmiter, R.D. (2015). Parabrachial calcitonin gene-related peptide neurons mediate conditioned taste aversion. J Neurosci 35**,** 4582-6.

Rabasa, C., Askevik, K., Schele, E., Hu, M., Vogel, H., and Dickson, S.L. (2019). Divergent Metabolic Effects of Acute Versus Chronic Repeated Forced Swim Stress in the Rat. Obesity (Silver Spring) 27**,** 427-433.