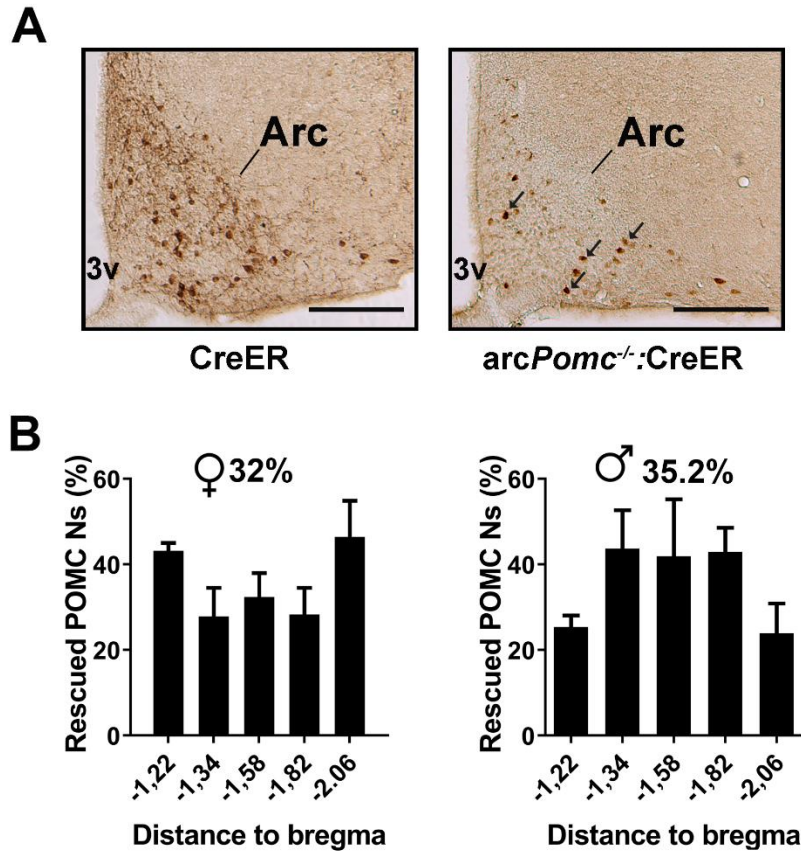
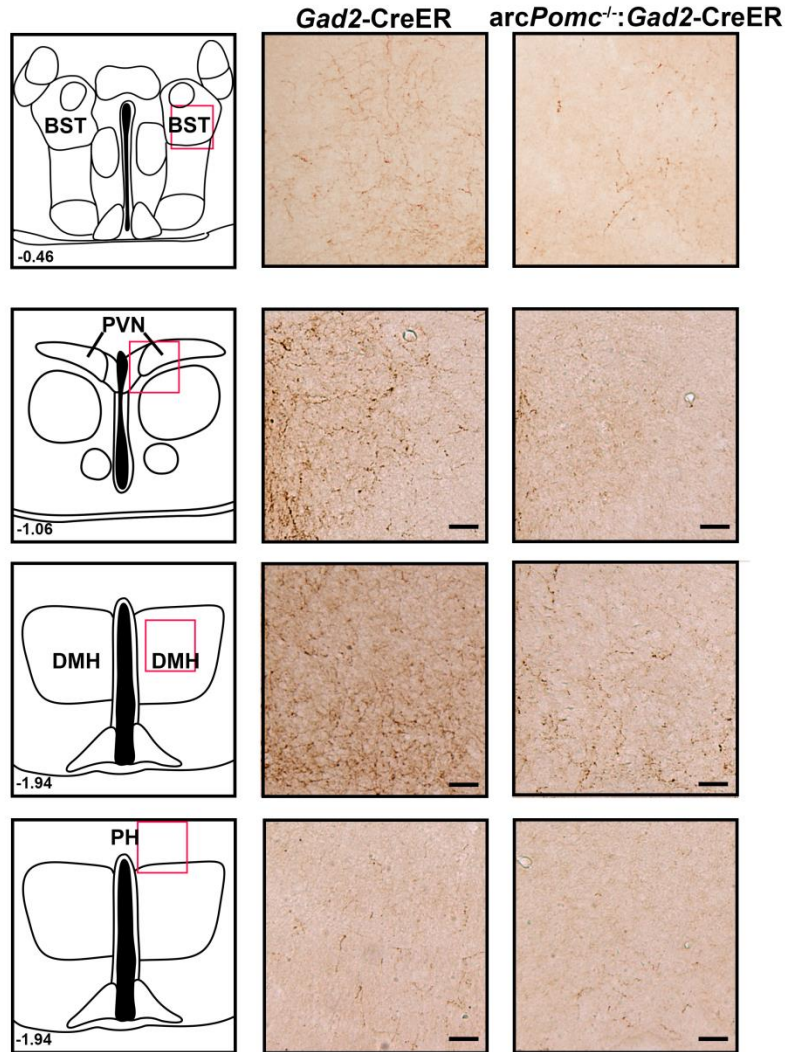


Supplementary Figure 1. *Pomc* rescue in GABAergic-POMC neurons improves glucose tolerance. Glucose Tolerance Tests (GTTs) before (PRE, 7th week of age) and after (POST, 14th week of age) tamoxifen treatment of female (A-D) and male (E-H) mice. (A, C, E, G) p: genotype effects of RMA. *arcPomc^{-/-}:Gad2-CreER* vs. *Gad2-CreER*: *p=0.05, **p=0.01, ***p=0.001 (Bonferroni). *arcPomc^{-/-}* vs. *Gad2-CreER*: #p=0.05, ##p=0.01, ###p=0.001 (Bonferroni). *arcPomc^{-/-}:Gad2-CreER* vs. *arcPomc^{-/-}*: ▲p=0.05. (B, D, F, H) Area under the curves (AUC) of A, C, E, G, respectively. OWA: *p=0.05, **p=0.01, ***p=0.001 (Bonferroni). N=5-9. Error bars correspond to ±SEM.



Supplementary Figure 2. POMC neurons partially rescued by a nonspecific Cre driver. (A) Representative coronal brain sections of CreER and partially rescued *arcPomc*^{-/-}:CreER mice showing ACTH immunopositive neurons. Arrows indicate neurons with rescued POMC expression. 3v, third ventricle. Arc, arcuate nucleus. Magnification bars: 200 μ m. (B) Percentages of POMC neurons in *arcPomc*^{-/-}:CreER rescued mice, relative to POMC neurons in CreER control mice, at different coronal levels of the hypothalamus. Rostro-caudal analysis shows no significant differences (OWA). Error bars: \pm SEM; n= 3.



Supplementary Figure 3. GABAergic-POMC fibers projecting to different brain areas of POMC rescued mice. Left column: Schematic coronal brain sections adapted from Paxinos G. et al, 2001 (The Mouse Brain in Stereotaxic Coordinates, 2nd edition). Red rectangles signalize brain areas shown in the two corresponding pictures on the right. Numbers indicate distances to bregma in mm. BST: Bed nucleus of the stria terminalis; PVN: Paraventricular hypothalamic nucleus; DMH: Dorsomedial hypothalamic nucleus; PH: Posterior hypothalamic nucleus. **Middle and right columns:** Representative coronal brain sections of control *Gad2-CreER* (middle column) and rescued *arcPomc^{-/-}:Gad2-CreER* (right column) female mice showing POMC immunoreactive fibers. Magnification bars: 50 μ m.