**Supplemental Figure 1.** Expression of insulin receptor (IR) in the mouse hypothalamus.

(Left) Representative coronal section of a mouse hypothalamus with DAB immunostaining for insulin receptor α subunit. (Right) Determination of the specificity of IRα antibody (Ab) using the blocking peptide (BP) competition assay (n=3 experiments per treatment). Scale bar = 250 μm. DMH, dorsomedial hypothalamus; VMH, ventromedial hypothalamus; ARC, arcuate nucleus of the hypothalamus; 3V, third ventricle.
Supplemental Figure 2. Determination of the specificity of IRα subunit antibody (Ab) by Western blot using the blocking peptide (BP) competition assay on mouse mediobasal hypothalamus protein lysates. IRα band (135 kDa, top blot) was absent when the IRα antibody was pre-incubated with the BP. However, pre-incubation of the BP with the IRβ antibody does not interfere with its immunoreactivity with the IRβ (95 kDa, bottom blot) (n=3 experiments per treatment).
**Supplemental Figure 3.** Effect of ICV rapamycin (1 ng) or vehicle (DMSO) on food intake (A,C) and body weight (B,D) in mice at 4 h (A,B) and 24 h (C,D) post-injection, n=4-7 mice per treatment. NS, not statistically significant.
Supplemental Figure 4. Effect of PI3K inhibition (LY294002) on insulin-induced activation of hypothalamic mTORC1 pathway in vitro. (A-D) Pre-treatment with LY294002 (10 μM, 20 min) blocked insulin activation of mTOR (A), S6K (B), S6 (C) and Akt (D) in GT1-7 cells, n=3-4 experiments per treatment. Values are mean ± SEM. *p<0.05 vs. other groups. #p<0.05 vs. Veh/Veh.