Supplementary Data

Obesity-induced Hepatic Steatosis is Mediated by Endoplasmic Reticulum Stress in the Subfornical Organ of the Brain

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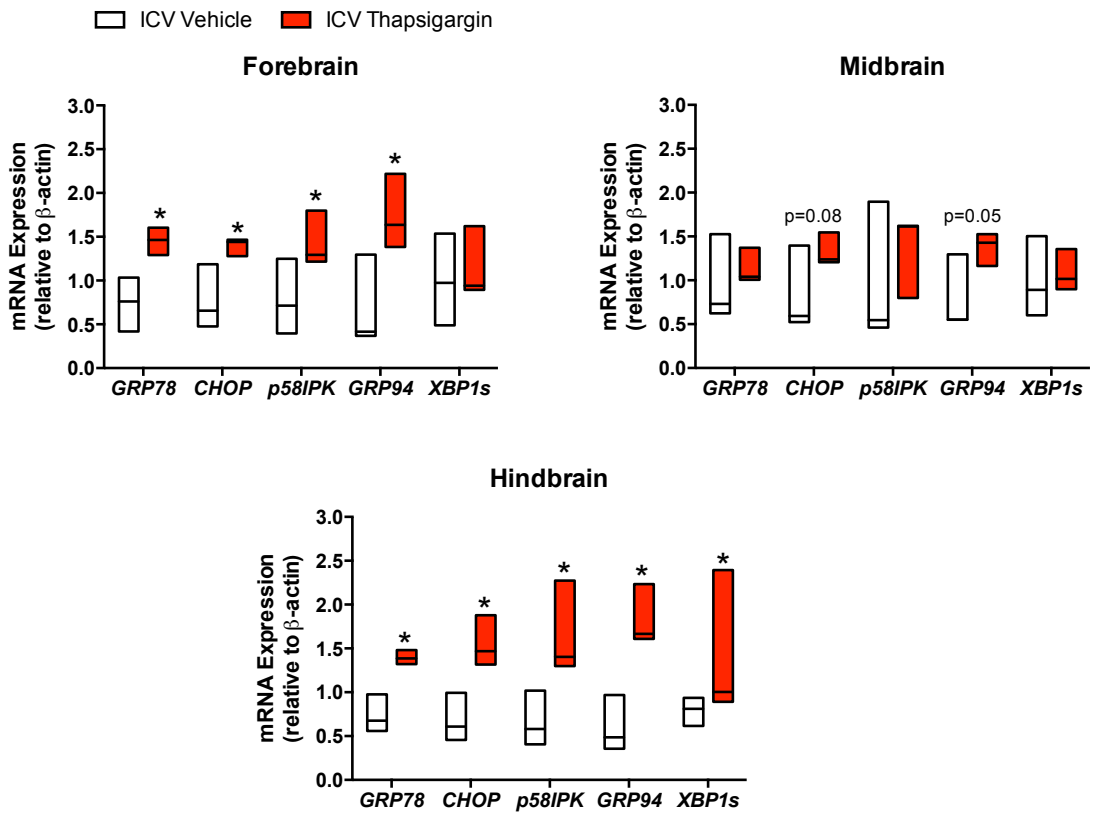
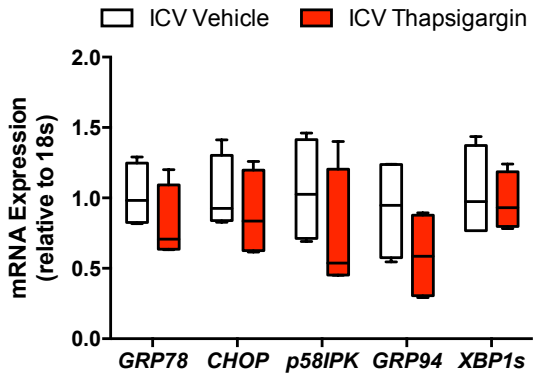
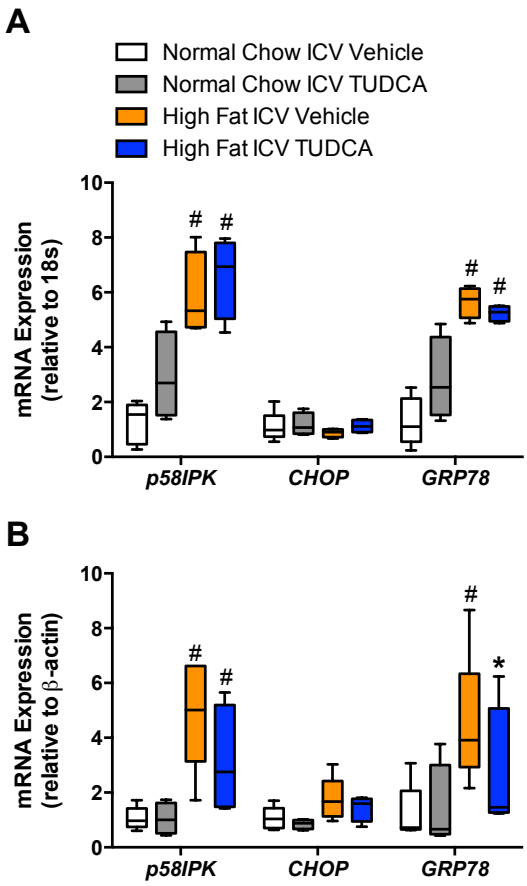


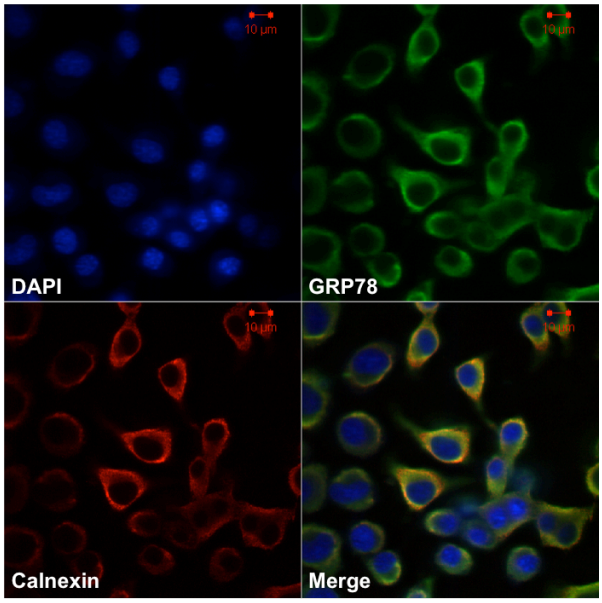
Supplemental Figure 1. Daily ICV administration of thapsigargin causes UPR activation in the brain. mRNA measurements of the ER stress markers *GRP78*, *CHOP*, *p58IPK*, *GRP94* and *XBP1s* in the forebrain, midbrain and hindbrain following 3 day ICV administration of the ER stress inducer thapsigargin or vehicle control. n=3/group. *p<0.05 vs. ICV Vehicle. Box plots represent the median (line within box) and upper and lower quartile (bounds of box).



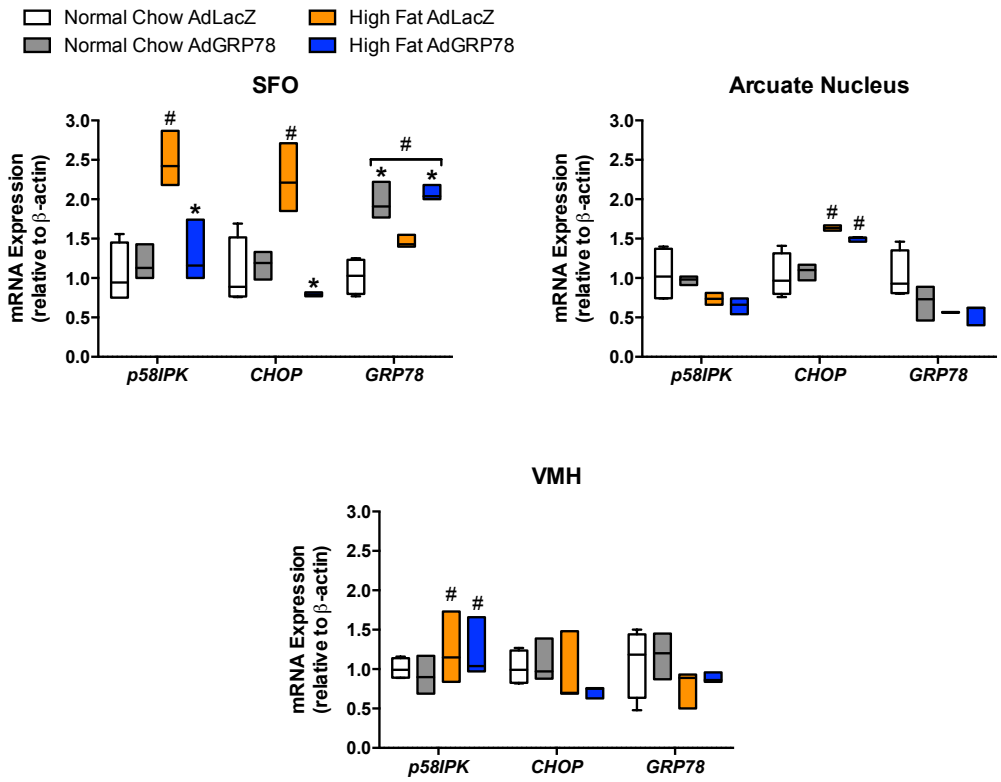
Supplemental Figure 2. Short-term induction of brain ER stress does not alter hepatic UPR markers. mRNA measurements of the ER stress markers *GRP78*, *CHOP*, *p58IPK*, *GRP94* and *XBP1s* in the liver following 3 day ICV administration of the ER stress inducer thapsigargin or vehicle control. n=4/group. Box-and-whisker plots represent the median (line within box), upper and lower quartile (bounds of box), and maximum and minimum values (bars).



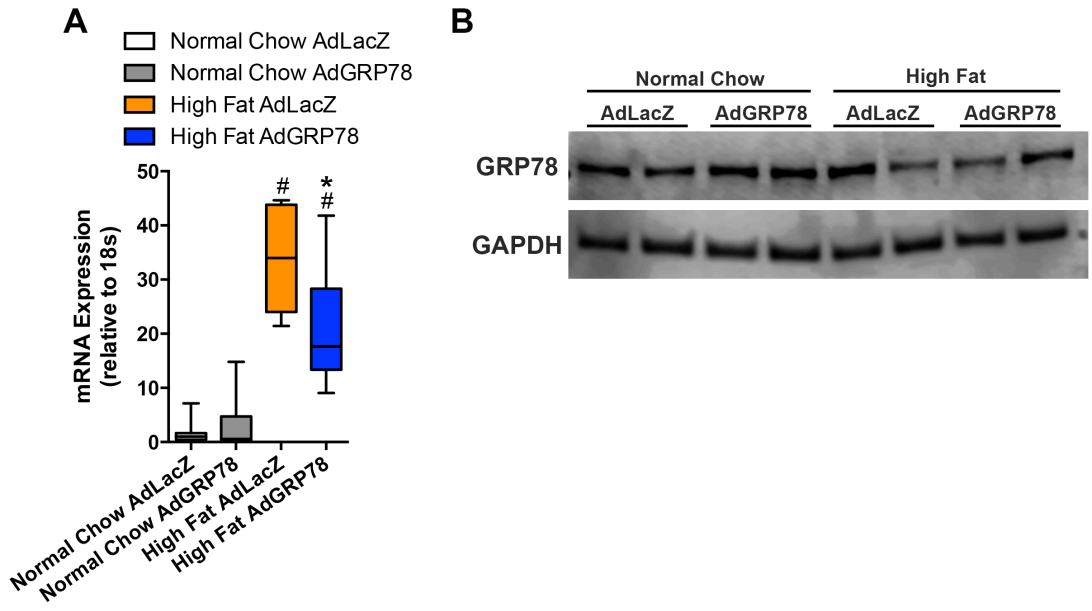
Supplemental Figure 3. Short-term ICV TUDCA reduces obesity-induced ER stress in the SFO, but not the liver. mRNA measurements of the ER stress markers *p58IPK*, *CHOP*, and *GRP78* in the liver (A) and SFO micropunches (B) following 3 day ICV administration of the ER stress chaperone TUDCA or vehicle control, in normal chow and HFD fed mice. n=6-8/group. #p<0.05 vs. Normal Chow groups; *p<0.05 vs. High Fat ICV TUDCA. Box-and-whisker plots represent the median (line within box), upper and lower quartile (bounds of box), and maximum and minimum values (bars).



Supplemental Figure 4. Adenoviral overexpression of GRP78 (AdGRP78) is targeted to the ER. Immunohistochemistry of Neuro2A cells transfected with AdGRP78 demonstrating localization of the transgene to the ER, as indicated by co-labeling with the ER marker calnexin. Scale bar = 10 μm.



Supplemental Figure 5. SFO-targeted adenoviral overexpression of GRP78 reduces obesity-induced ER stress in the SFO but not mediobasal hypothalamus. mRNA measurements of the ER stress markers *p58IPK*, *CHOP* and *GRP78* following SFO-targeted AdGRP78, or control AdLacZ, in normal chow and HFD fed mice. VMH, ventromedial hypothalamus. n=3-4/group, 2 brains pooled per sample. #p<0.05 vs. Normal Chow groups; *p<0.05 vs. High Fat AdLacZ. Box-and-whisker plots represent the median (line within box), upper and lower quartile (bounds of box), and maximum and minimum values (bars).



Supplemental Figure 6. SFO-targeted adenoviral overexpression of GRP78 does not increase liver GRP78 expression. (A) Liver mRNA measurements of *GRP78* following SFO-targeted AdGRP78, or control AdLacZ, in normal chow and HFD fed mice. n=6-8/group. #$p<0.05$ vs. Normal Chow groups; *$p<0.05$ vs. High Fat AdLacZ. Box-and-whisker plots represent the median (line within box), upper and lower quartile (bounds of box), and maximum and minimum values (bars). (B) Western blot of liver GRP78 following SFO-targeted AdGRP78, or control AdLacZ, in normal chow and HFD fed mice.