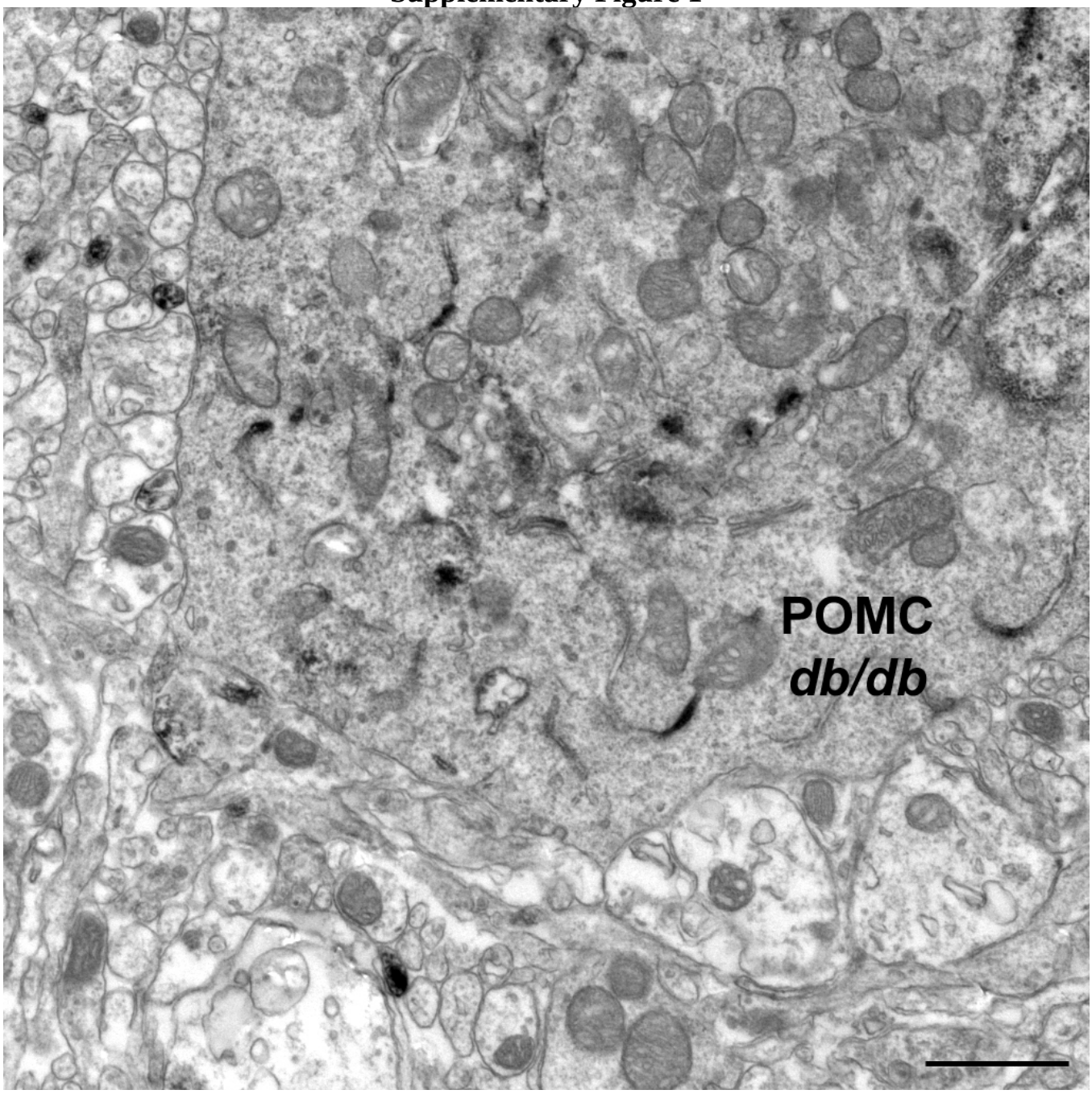
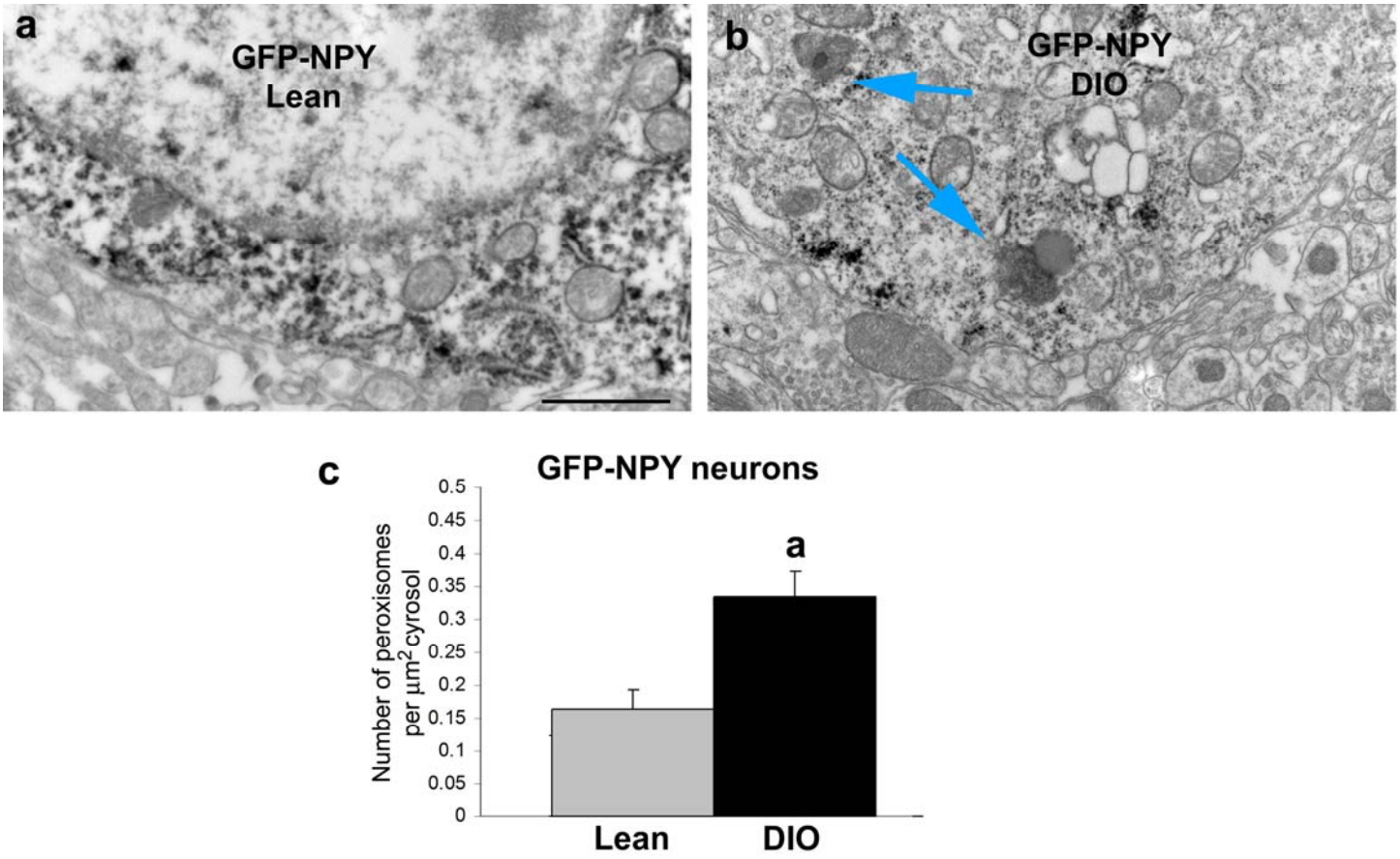
Supplementary Figure 1



Supplementary Fig. 1

Electron micrograph of a POMC perikarion from a *db/db* mouse. Note the lack of peroxisome presence in this cell. Bar scale represents 1 μm.

Supplementary Figure 2

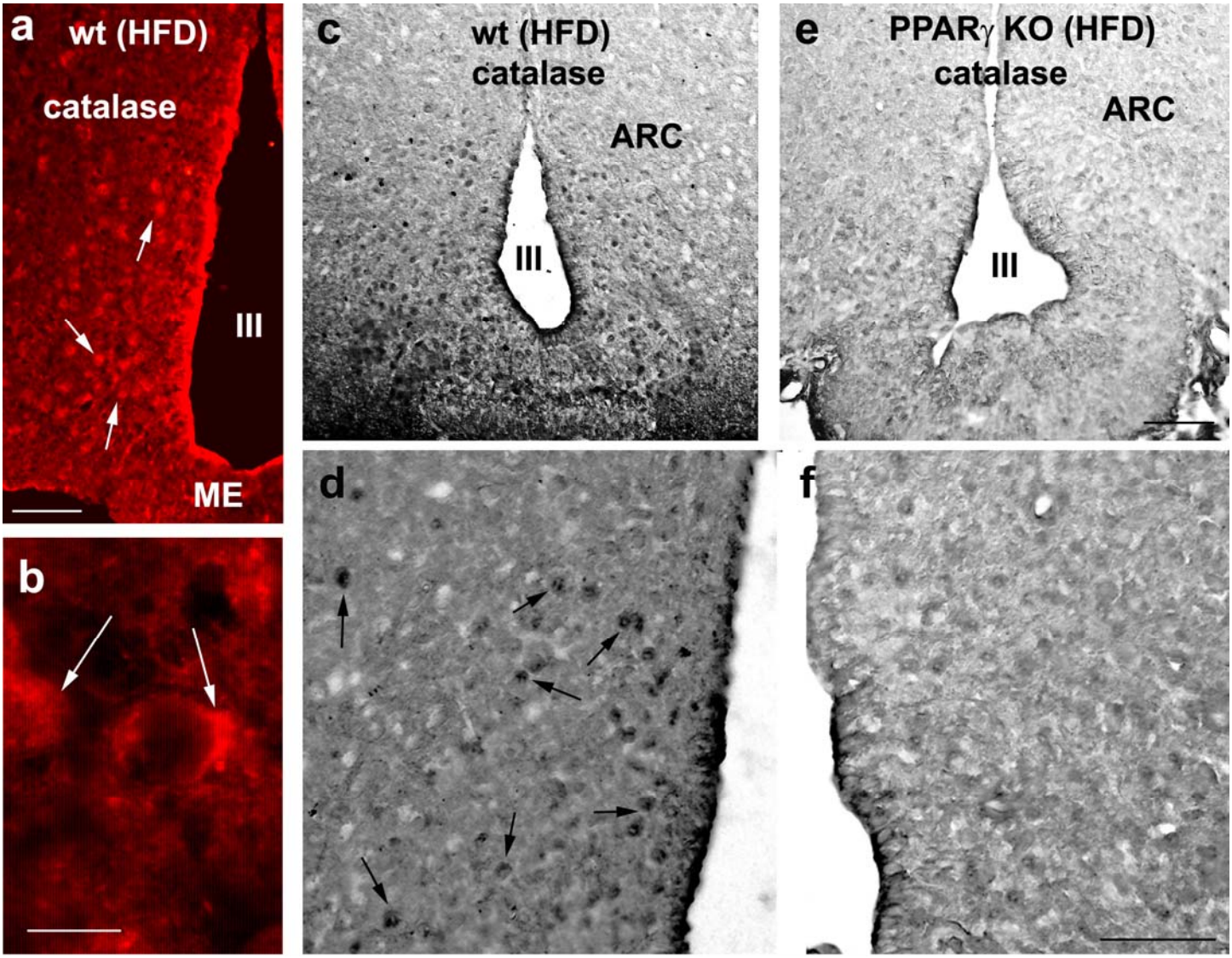


Supplementary Fig. 2

a, b: electron micrographs of NPY-GFP perikarya from a lean (**a**) and a DIO animal (**b**). Peroxisomes (blue arrows on **b**) are readily visible in DIO NPY neurons. Bar scale on a represent 1 µm for panels **a** and **b**.

c: Quantification of peroxisome number showed significantly higher number of peroxisomes in arcuate NPY neurons of DIO mice compared to lean controls. * indicate $p<0.05$.

Supplementary Figure 3

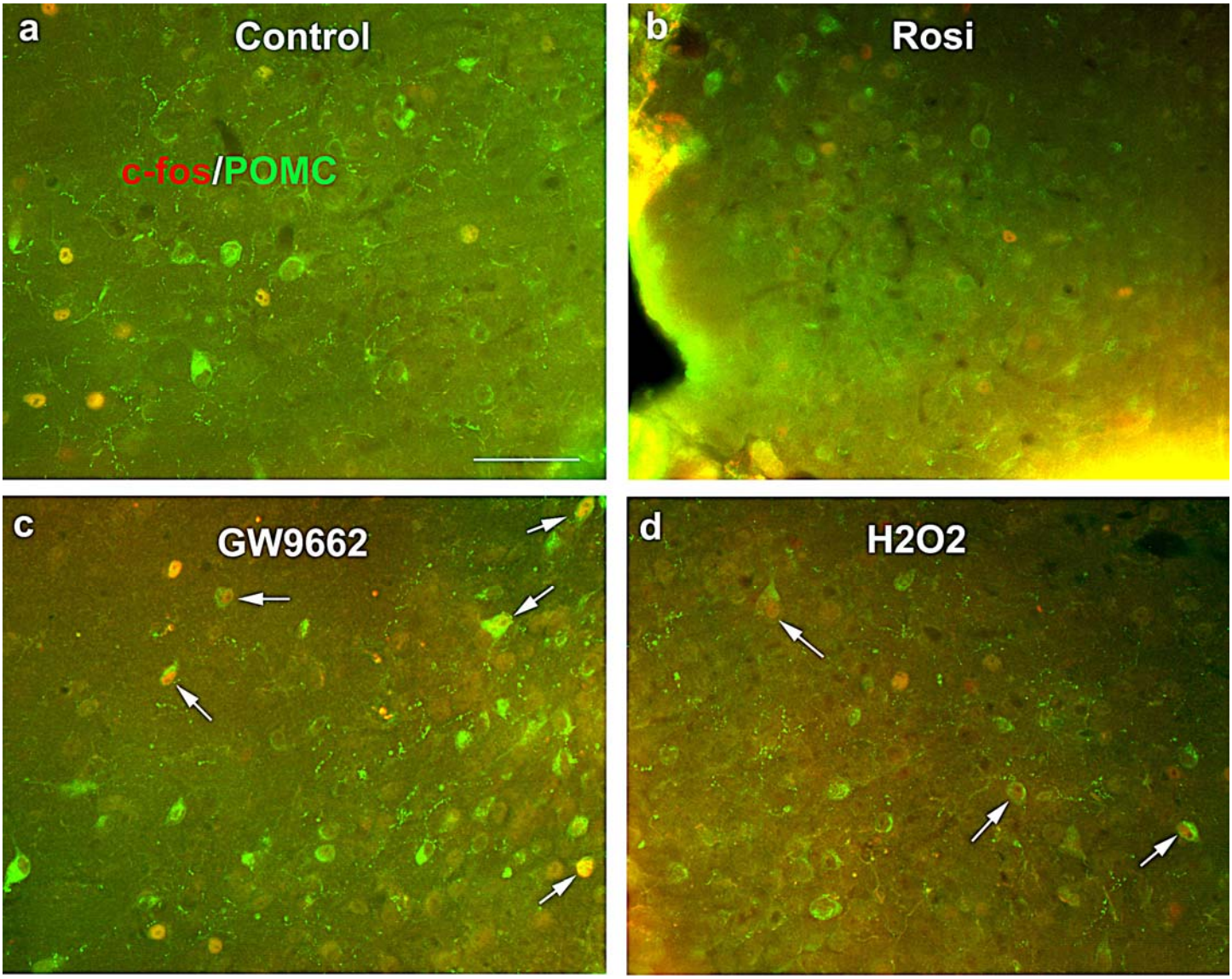


Supplementary Fig. 3

a,b: immunofluorescence labeling for catalase revealed labeled cells in the hypothalamus of wild type animals on high fat diet. Arrows point to labeld cells. On **b**, the subcellular labeling of catalase indicate punctuate cytoplasmic labeling. Bar scale on **a** indicates 100 μm. Bar scale on **b** indicate 10 μm.

c-f: Immunolabeleing with avidin-biotin peroxidase revelaes numerous catalase immunoporitive cells of the arcuate nucleus of wild type mice on high fat diet (**c** and **d**), while catalase immunolabeleing was substantially lower in the arcuate nucleus of neuron-specifc PPARγ knockout mice (**e** and **f**). Bar scales on **e** represents 100 μm for panels **c** and **e**, and, on **f**, it represents 100 μm for panels **d** and **f**.

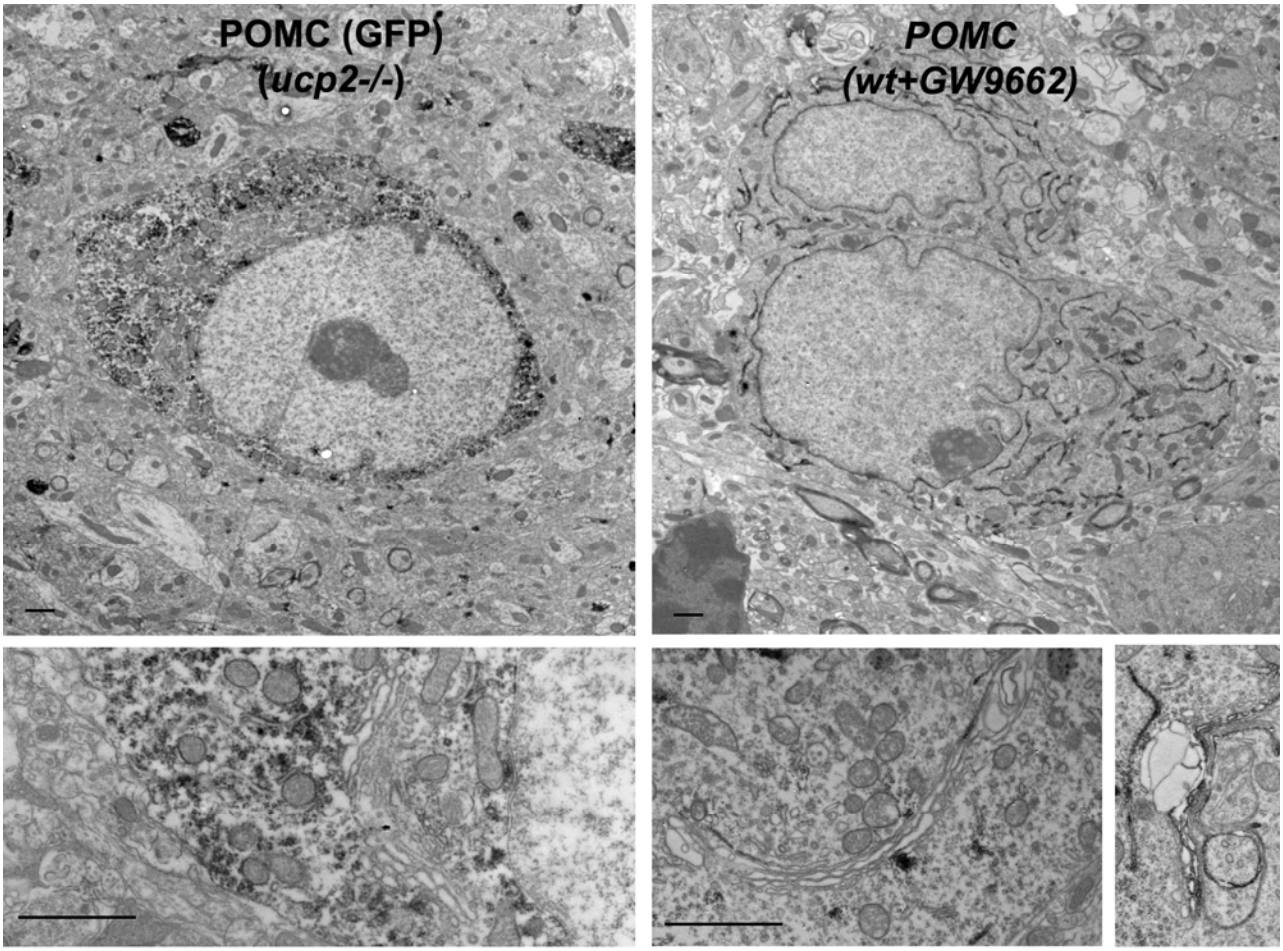
Supplementary Figure 4

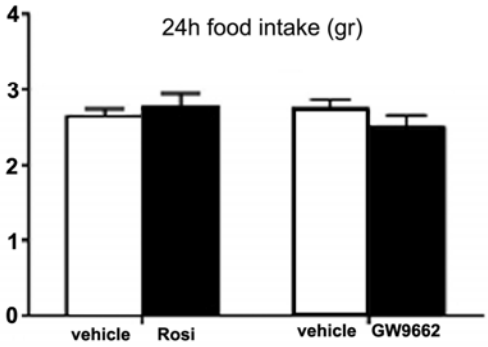


Supplementary Fig. 4

a-d: double immunofluorescence labeling for c-fos (red) and POMC (green) from control DIO (**a**), rosigliatzone-treated (**b**), GW9662-treated (**c**) and H2O2-treated (**d**) high fat-fed animals. Bar scale on **a** represents 100 μm for panels **a-d**.

Supplementary Figure 5





Supplementary Fig. 5

Electron migrographs showing a POMC neuron (GFP-POMC) from a UCP2 knockout mouse (left panels) and from a DIO mouse (immunolabaled for POMC) treated with GW9662 (right panels). Note the similarity in cell integrity, abundance of endoplasmic reticulum (lower panels) and low incidence of peroxisomes. Lower right panel shows an endoplasmic reticulum with lipid accumulation. Peroxisomes would bud off the endoplasmic reticulum in response to lipid overload. Bar scales indicate 1 μm. Bar graphs show that neirher rosiglitazone nor GW9662 affected feeding in UCP2 knockout mice. Bar graphs show lack of effect of either rosiglitazone or GW9662 on daily food intake of UCP2 knockout mice.