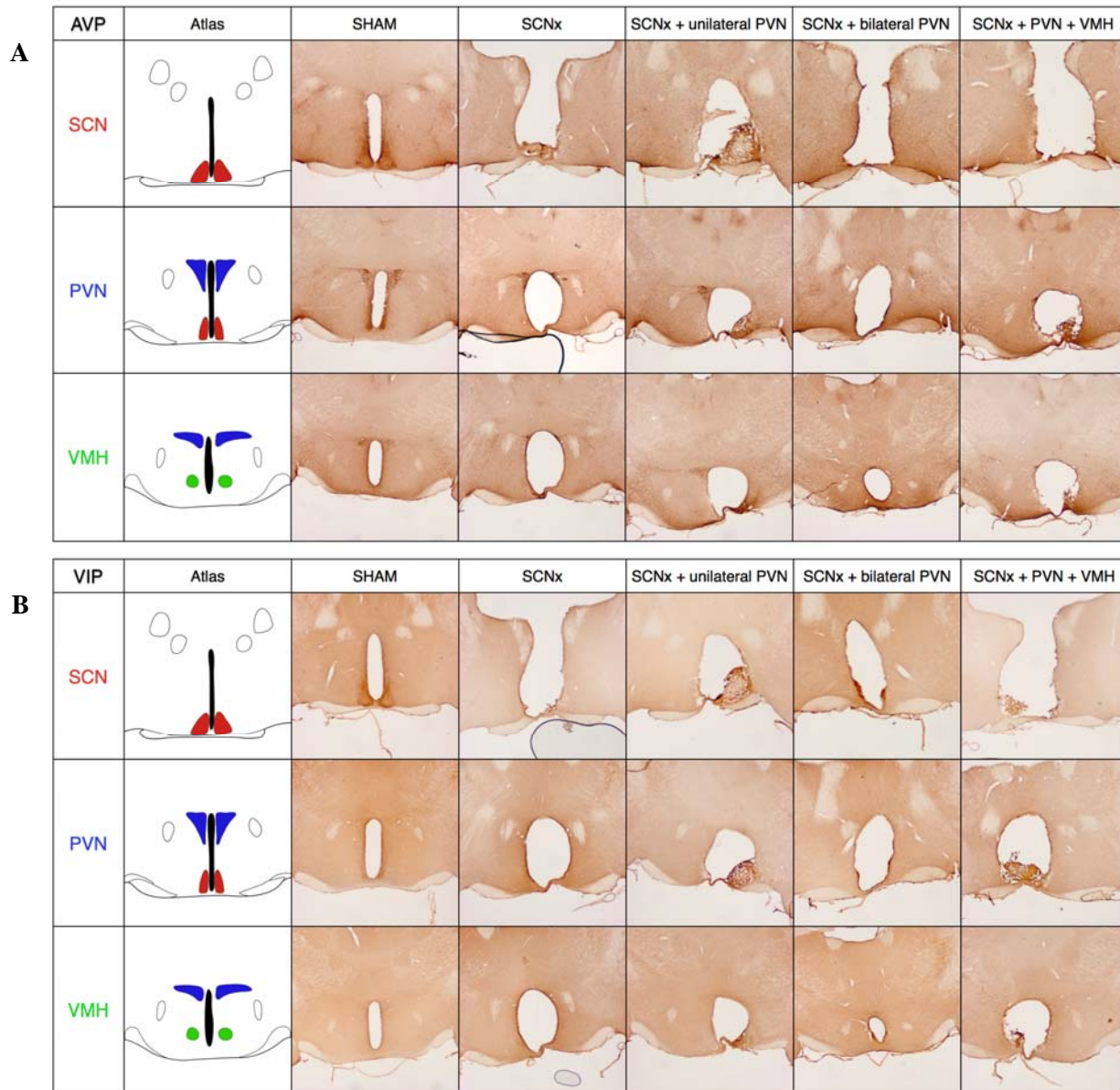
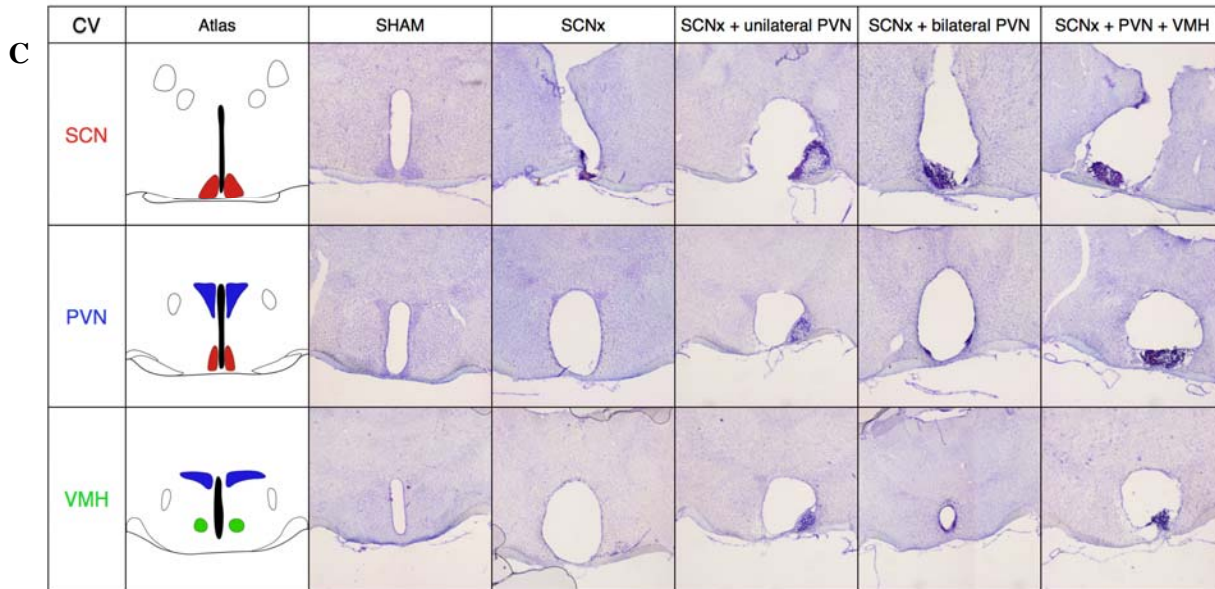


SUPPLEMENTARY DATA

Supplementary Figure 1. Representative histological sections of the hypothalamus, illustrating the histological verification of lesion position and size. 40 micrometer coronal sections were alternately stained for arginine vasopressin (AVP, immuno-histochemical staining, panel A), vasoactive intestinal peptide (VIP, immuno-histochemical staining, panel B) and cresyl violet (CV, cell-nuclei staining, panel C). For each animal, the location of lesion-induced damage was judged by independent researchers. Animals were classified based on (I) the presence of a bilateral ablation of the suprachiasmatic nucleus (SCN, top row of each panel) and for the presence of additional damage: (II) unilateral or bilateral ablation of the paraventricular nucleus (PVN, middle row in each panel) and (III) damage to the rostral part of the ventromedial hypothalamus (VMH, bottom row in each panel). For comparison, schematic drawings of the mouse hypothalamus (first column) and stainings of sham-operated animals (second column) are included.



SUPPLEMENTARY DATA



Supplementary Table 1. Glucose (A) and tracer specific activity (B) data for all groups during the basal and hyperinsulinemic period of the clamp. Data are represented as mean \pm SD.

A

| | Basal 1 [Glucose] (mmol/l) | Basal 2 [Glucose] (mmol/l) | Hyper 1 [Glucose] (mmol/l) | Hyper 2 [Glucose] (mmol/l) | Hyper 3 [Glucose] (mmol/l) |
|-----------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
| Sham | 5.0 \pm 0.7 | 4.9 \pm 1.0 | 4.6 \pm 0.8 | 4.7 \pm 1.0 | 4.7 \pm 1.0 |
| SCNx | 6.6 \pm 1.1 | 6.8 \pm 1.4 | 7.4 \pm 1.3 | 6.7 \pm 1.1 | 6.8 \pm 1.1 |
| SCNx + unilat PVN damage | 6.7 \pm 0.6 | 7.3 \pm 2.0 | 7.0 \pm 1.1 | 7.1 \pm 1.2 | 7.1 \pm 1.2 |
| SCNx + bilat PVN damage | 7.2 \pm 0.9 | 7.4 \pm 1.5 | 7.2 \pm 0.7 | 7.2 \pm 0.9 | 7.2 \pm 1.3 |
| SCNx + PVN/VMH damage | 7.6 \pm 1.7 | 7.6 \pm 1.9 | 6.8 \pm 1.0 | 7.4 \pm 1.7 | 7.4 \pm 1.6 |

B

| | Basal 1 SA (DPM/ μ mol) | Basal 2 SA (DPM/ μ mol) | Hyper 1 SA (DPM/ μ mol) | Hyper 2 SA (DPM/ μ mol) | Hyper 3 SA (DPM/ μ mol) |
|-----------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|--------------------------------|
| Sham | 12100 \pm 3966 | 12855 \pm 4176 | 7831 \pm 2283 | 7519 \pm 2587 | 7398 \pm 1990 |
| SCNx | 8849 \pm 1828 | 8891 \pm 1803 | 6066 \pm 283 | 5452 \pm 1044 | 6659 \pm 1241 |
| SCNx + unilat PVN damage | 9925 \pm 2274 | 9383 \pm 2606 | 6842 \pm 1804 | 7085 \pm 1365 | 7109 \pm 2013 |
| SCNx + bilat PVN damage | 6450 \pm 1098 | 6887 \pm 1864 | 5775 \pm 1339 | 6031 \pm 1625 | 6755 \pm 2227 |
| SCNx + PVN/VMH damage | 7532 \pm 4189 | 8174 \pm 5039 | 5302 \pm 1906 | 6068 \pm 2177 | 5920 \pm 2677 |

SUPPLEMENTARY DATA

Supplementary Table 2. Indirect calorimetry/metabolic cage (A), hyperinsulinemic-euglycemic clamp (B) and plasma insulin data of sham and SCN lesioned (SCNx) mice with collateral damage. Data are represented as mean \pm SD, * $P < 0.05$ vs. sham, ** $P < 0.01$ vs. sham, # $P < 0.05$ light vs. dark, § $P < 0.05$ basal vs. hyperinsulinemic-euglycemic clamp period.

| A <i>Dark</i> | | | |
|--------------------------|------------------------------|---|--|
| | VO2 (ml/kg/h) | Activity (bb/12 h) | FI (g/12 h) |
| Sham | 3386 \pm 173 | 195 \pm 67 | 3.20 \pm 0.53 |
| SCNx + unilat PVN damage | 3107 \pm 162* | 74 \pm 22* | 2.24 \pm 0.54* |
| SCNx + bilat PVN damage | 2530 \pm 196* | 61 \pm 23* | 2.52 \pm 0.73* |
| SCNx + PVN/VMH damage | 2594 \pm 513* | 57 \pm 29* | 2.42 \pm 0.72* |
| <i>Light</i> | | | |
| | VO2 (ml/kg/h) | Activity (bb/12 h) | FI (g/12 h) |
| Sham | 2992 \pm 154 [#] | 79 \pm 32 [#] | 1.53 \pm 0.23 [#] |
| SCNx + unilat PVN damage | 3130 \pm 200 | 92 \pm 41 | 2.27 \pm 0.92* |
| SCNx + bilat PVN damage | 2600 \pm 167* | 93 \pm 34 [#] | 1.60 \pm 0.38 |
| SCNx + PVN/VMH damage | 2579 \pm 495* | 73 \pm 45 | 2.27 \pm 0.55* |
| <i>24 h</i> | | | |
| | VO2 (ml/kg) | Activity (bb) | FI (g) |
| Sham | 76531 \pm 3831 | 273 \pm 123 | 4.73 \pm 0.50 |
| SCNx + unilat PVN damage | 74849 \pm 4302 | 166 \pm 62* | 4.51 \pm 1.43 |
| SCNx + bilat PVN damage | 61561 \pm 4327* | 154 \pm 55* | 4.13 \pm 1.06 |
| SCNx + PVN/VMH damage | 62075 \pm 12070* | 131 \pm 73* | 4.69 \pm 0.84 |
| B | | | |
| | Basal Rd (μ mol/min/kg) | Hyperinsulinemic Rd (μ mol/min/kg) | Hyperinsulinemic EGP (μ mol/min/kg) |
| Sham | 53.6 \pm 16.6 | 83.9 \pm 23.8 | 8.8 \pm 12.2 |
| SCNx + unilat PVN damage | 61.1 \pm 17.9 | 77.5 \pm 31.6 | 36.2 \pm 29.3* |
| SCNx + bilat PVN damage | 61.0 \pm 9.5 | 61.7 \pm 21.1* | 37.8 \pm 18.3* |
| SCNx + PVN/VMH damage | 51.2 \pm 24.4 | 55.6 \pm 19.8* | 40.2 \pm 23.1* |

SUPPLEMENTARY DATA

C

| | Insulin (ng/ml) | |
|--------------------------|-------------------------|---------------------------|
| | Basal | Hyperinsulinemic |
| Sham | 0.5 ± 0.3 | 5.2 ± 1.1 ^{\$} |
| SCNx + unilat PVN damage | 0.8 ± 0.3 | 4.8 ± 1.1 ^{\$} |
| SCNx + bilat PVN damage | 2.9 ± 1.5 ^{**} | 8.6 ± 2.4 ^{\$**} |
| SCNx + PVN/VMH damage | 1.4 ± 0.6 ^{**} | 4.6 ± 1.7 ^{\$} |