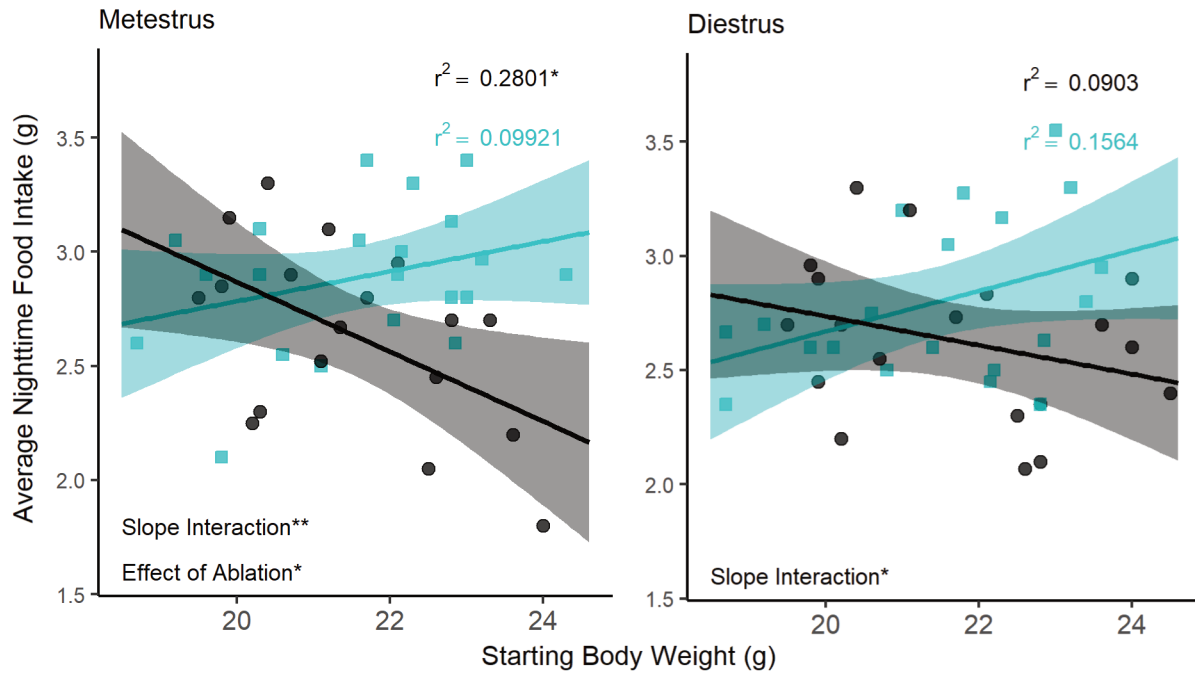


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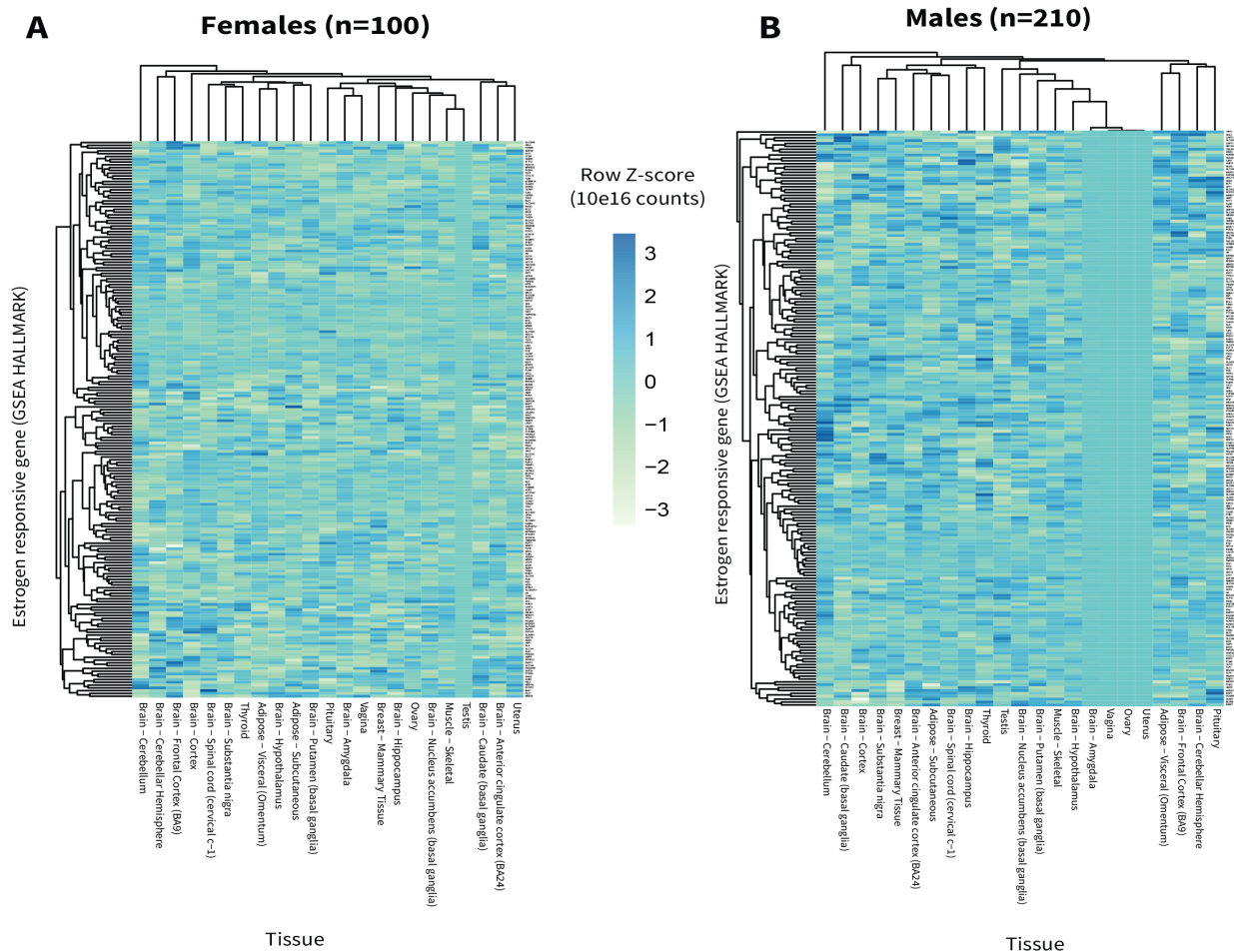
Supplementary Figure 1 (companion to Figure 2): TN^{SST} neuronal ablation does not affect any other metabolic measures studied. Telemetry measures of (A) activity and (B) core body temperature are unaffected by TN^{SST} neuronal ablation. (C) Fasting glucose tolerance test is also unaffected by TN^{SST} neuron ablation. (D) Despite changes to food intake, ablation does not affect body weight over time. Mean ± SEM; *, p<0.5; ***, p<0.001. M Control n=9; M Ablated n=9; F Control n=5; F Ablated n=7. Pro: Proestrus, Est: Estrus, Met: Metestrus, Di: Diestrus.



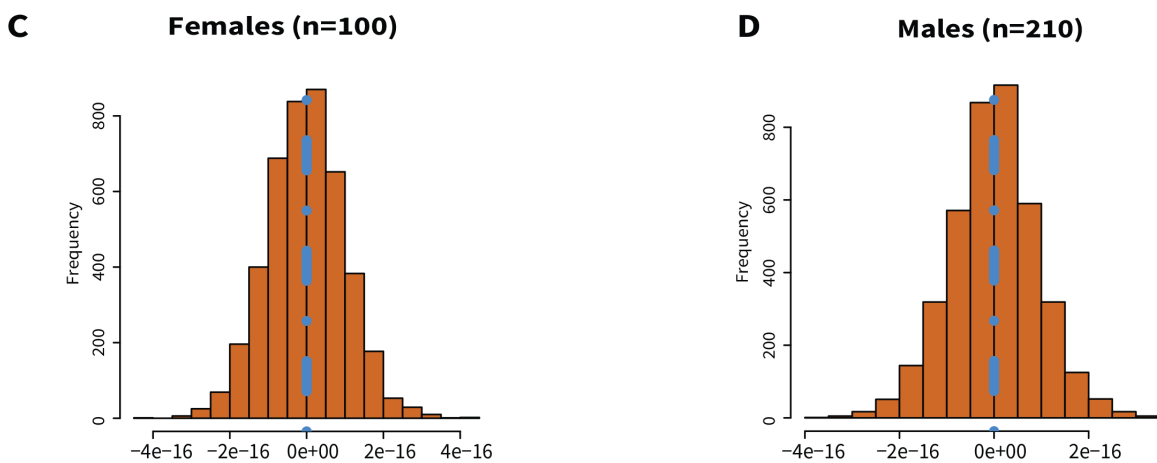
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Supplementary Figure 2 (companion to Figure 3). (A) Regression analysis of food intake and body mass across all ovary-intact animals in metestrus (left panel) and diestrus (right panel) reveals an interaction between body mass and nightly food intake in females. Significant negative correlations in wildtype animals (black line, round black dots) are seen in the higher estradiol phase of metestrus but not in caspase ablated females (cyan line, square cyan points). Metestrus: Control n=18, Ablated n=21; Diestrus: Control n=19, Ablated n=20.

Pan-tissue estrogen binning



Gene-tissue z-score distribution



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499 **Supplementary Figure 3 (companion to Figure 5).** (A&B) Z-scores of estrogen signaling genes (y-axis, [https://www.gsea-](https://www.gsea-msigdb.org/gsea/msigdb/cards/HALLMARK_ESTROGEN_RESPONSE_EARLY.html)
500 [msigdb.org/gsea/msigdb/cards/HALLMARK_ESTROGEN_RESPONSE_EARLY.html](https://www.gsea-msigdb.org/gsea/msigdb/cards/HALLMARK_ESTROGEN_RESPONSE_EARLY.html)) across indicated tissues (x-axis) in
501 GTEx female (no Y chromosome, A) and male (Y chromosome present, B) individuals. (C&D) Based on the distributions of
502 these scores across relevant metabolic tissues, individuals were segregated into categories of “low” (<0, left of blue line) or
503 “high” (>0, right of blue line) estrogen signaling and used for cross-tissue genetic correlations.