

Preoptic PNOc Neurons Modulate Energy Balance and Adipose Tissue Function

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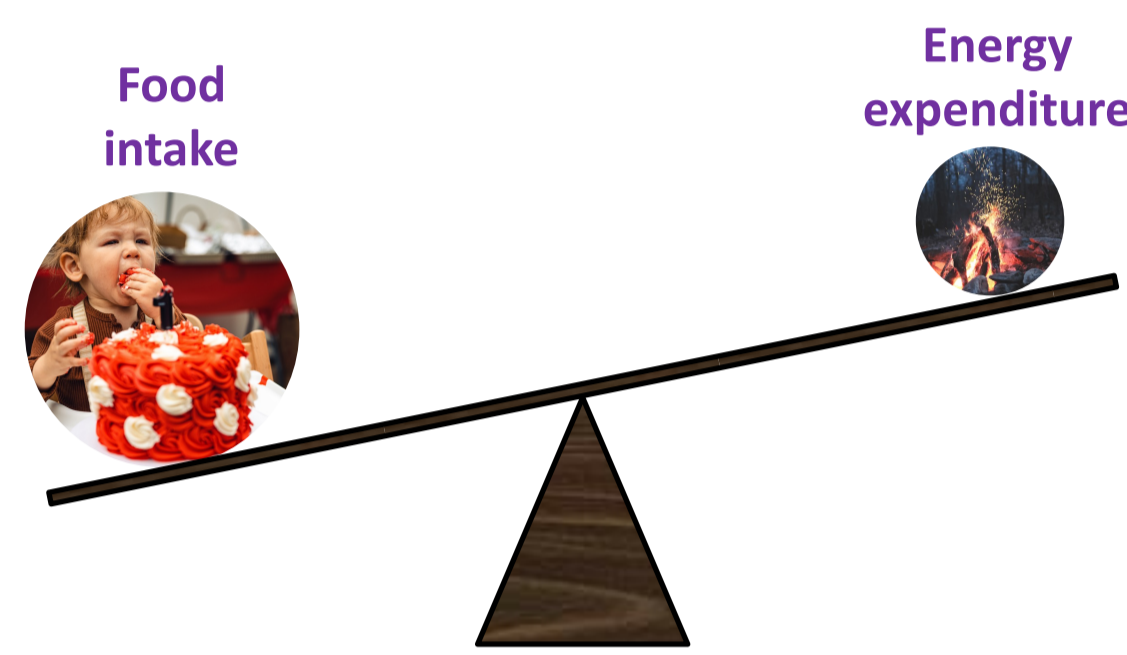
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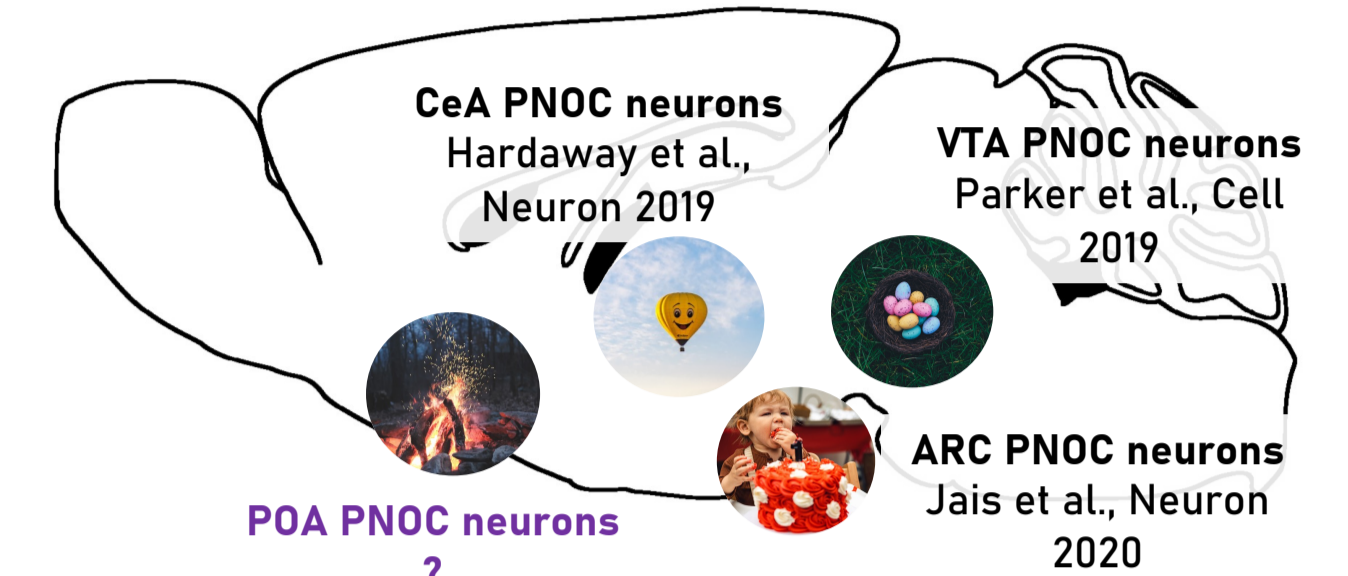
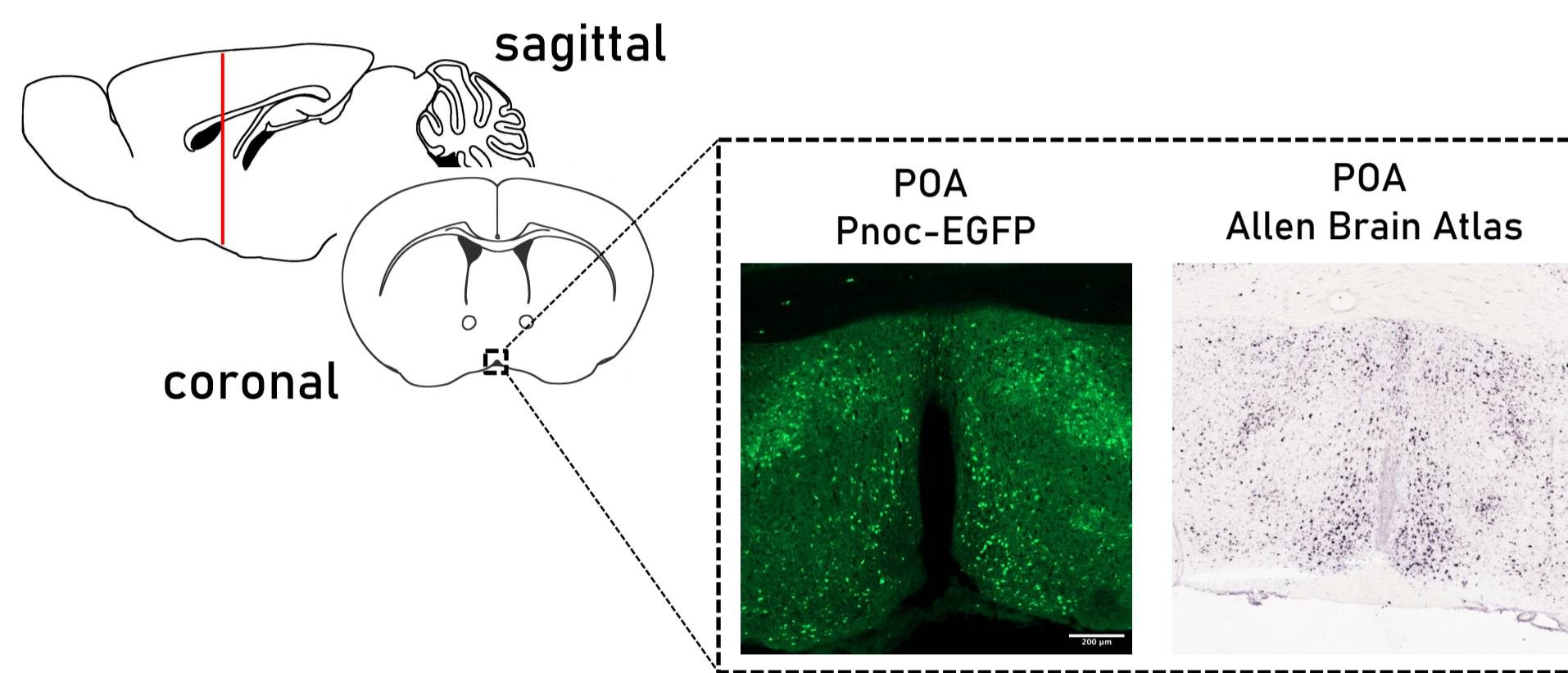
Background

The central nervous system constantly monitors and integrates metabolic signals to maintain energy homeostasis. A well-defined neurocircuit in this context is the melanocortin system. However, it's worth noting that overnutrition may also engage other neurocircuits. Recent studies have shown that neurons expressing **prepronociceptin (PNOc)** are activated in response to the consumption of palatable, energy-dense foods, leading to hyperphagia. Unravelling the complex relationship between food intake and energy expenditure is crucial for understanding the mechanisms underlying metabolic control.



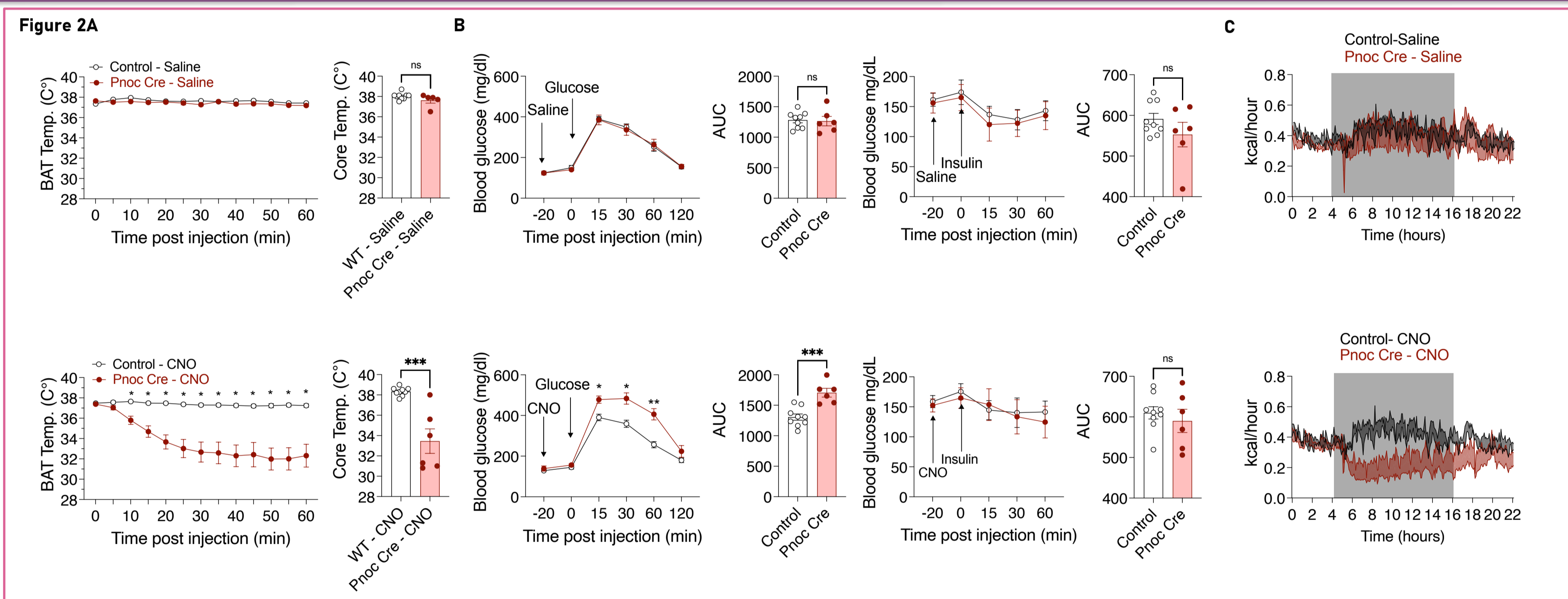
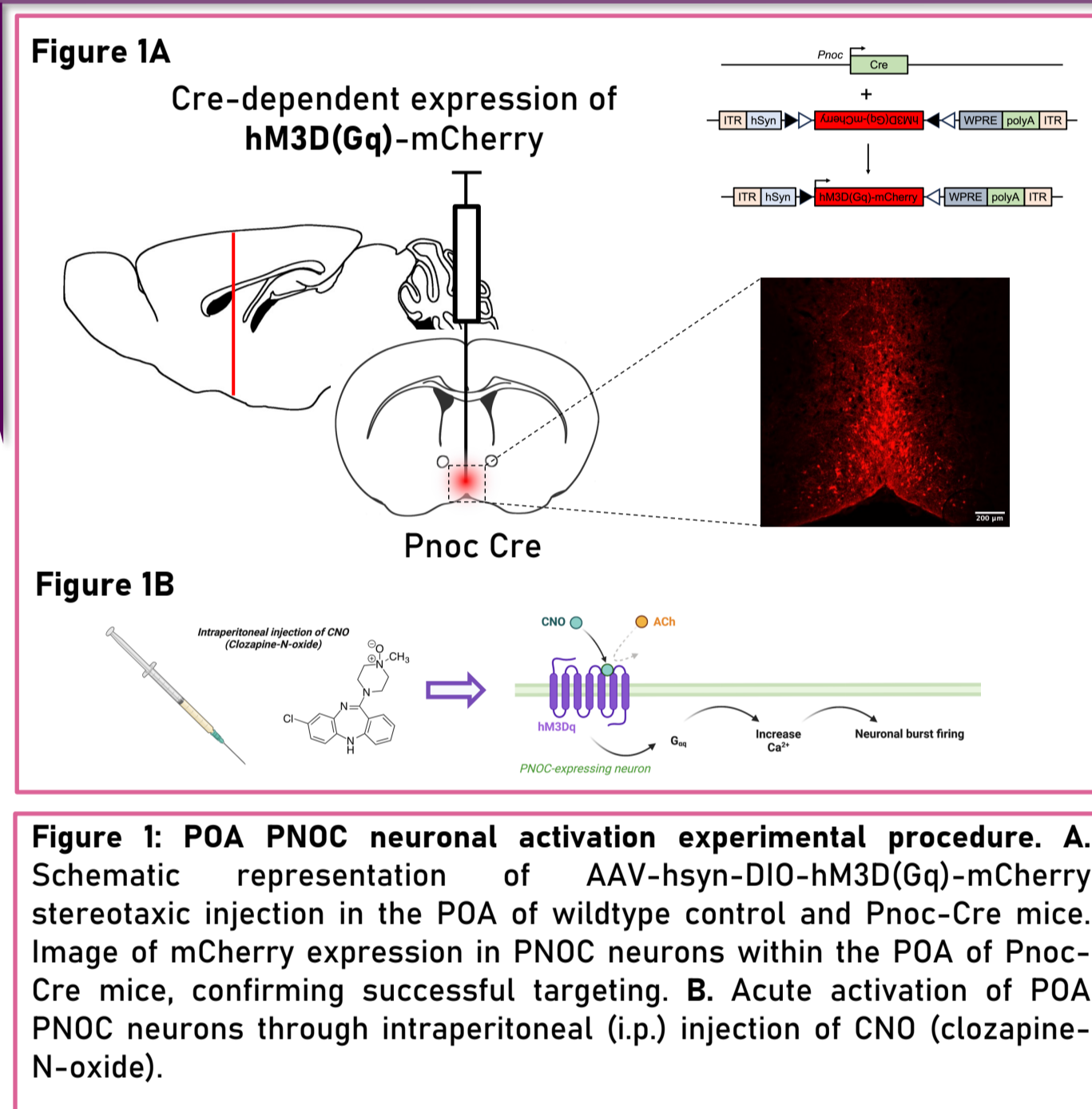
Here, we are characterizing the role of PNOc-expressing neurons in the preoptic area of the hypothalamus in the regulation of energy storage and expenditure.

We hypothesize that POA PNOc neurons play a crucial role in orchestrating a metabolic shift towards energy storage. This shift is achieved by downregulating the activity of thermogenic tissues, such as brown adipose tissue (BAT), leading to a reduction in overall energy expenditure.

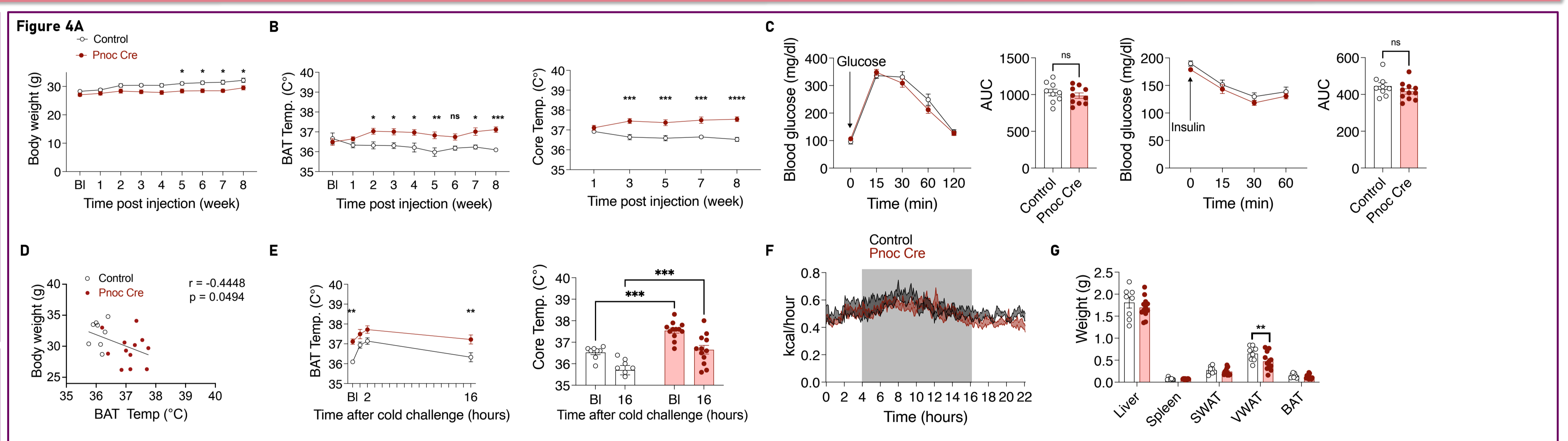
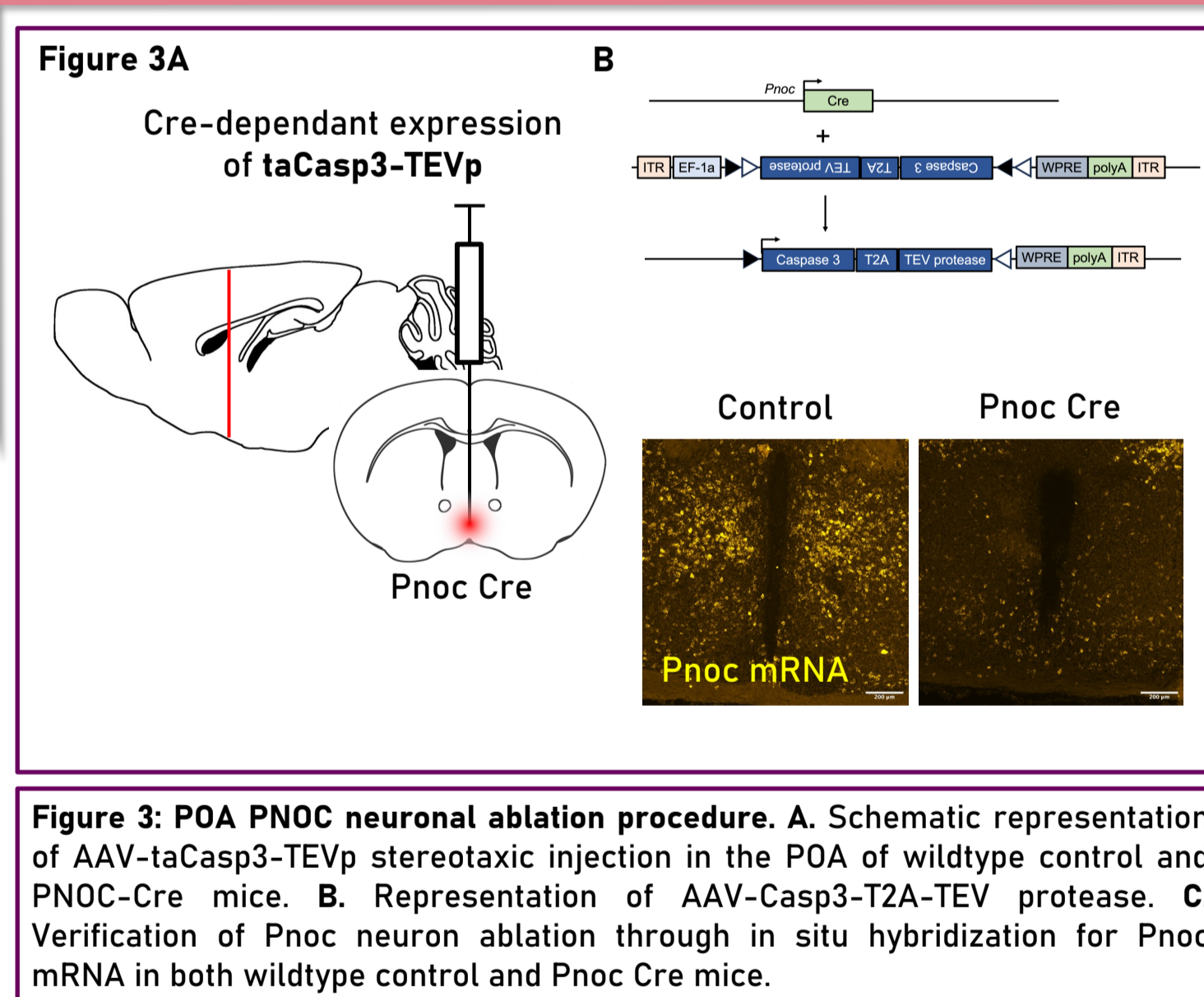


PNOc neurons in the arcuate nucleus (ARC) of the hypothalamus are activated upon high-fat diet feeding and activation of ARC PNOc neurons promotes feeding via inhibition of anorexigenic proopiomelanocortin (POMC)-expressing neurons. In the central amygdala (CeA) PNOc neurons stimulate reward sensation after intake of palatable food. In the ventral tegmental area (VTA) PNOc neurons regulate food foraging via interaction with VTA dopamine neurons. However, the role of preoptic (POA) PNOc neurons is unknown.

Acute activation of POA PNOc neurons decreases BAT thermogenesis and energy expenditure



Ablation of POA PNOc neurons increases BAT thermogenesis and reduces body weight



POA PNOc neuronal activation acutely upregulates pro-inflammatory markers in adipose tissue

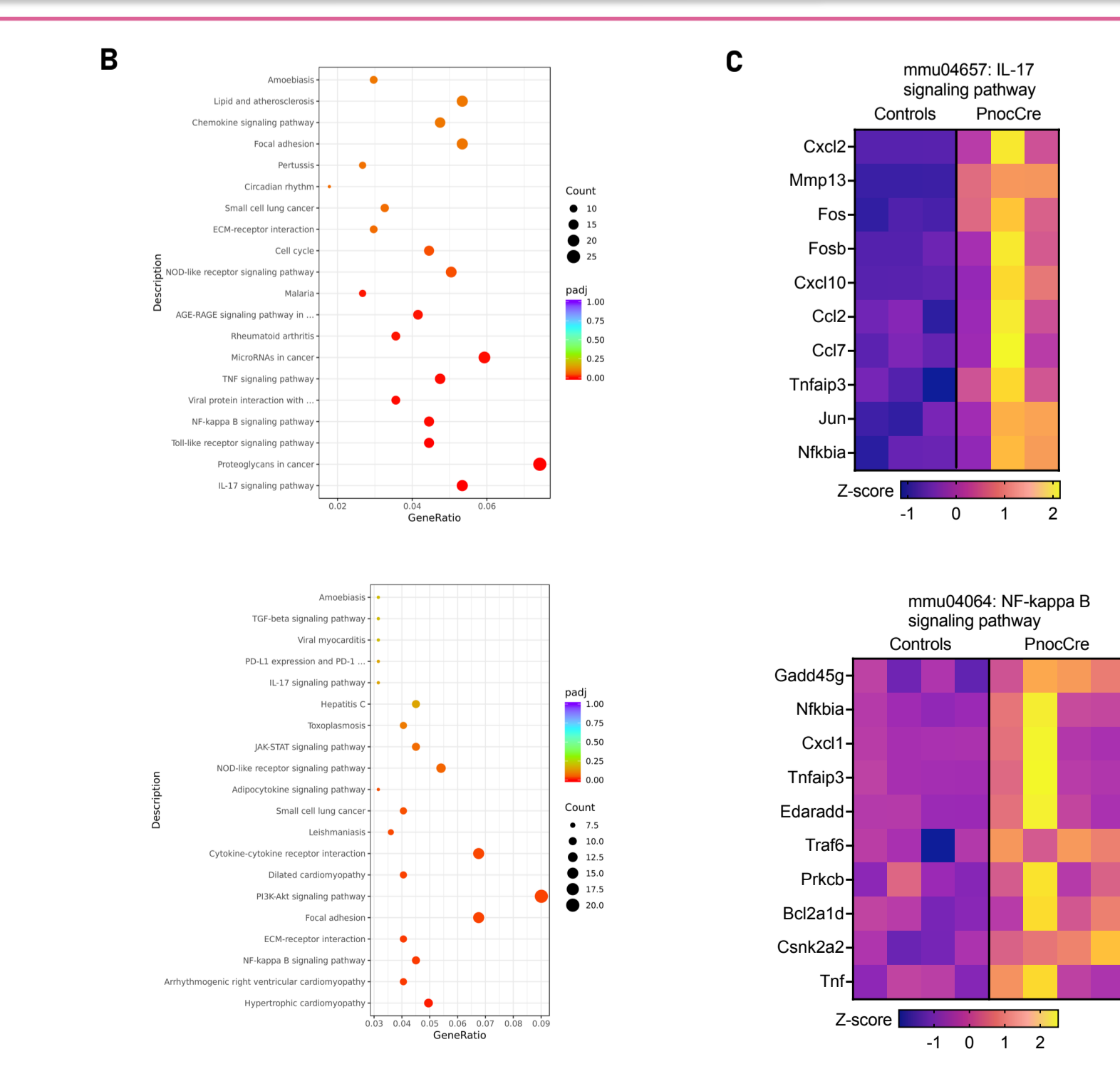
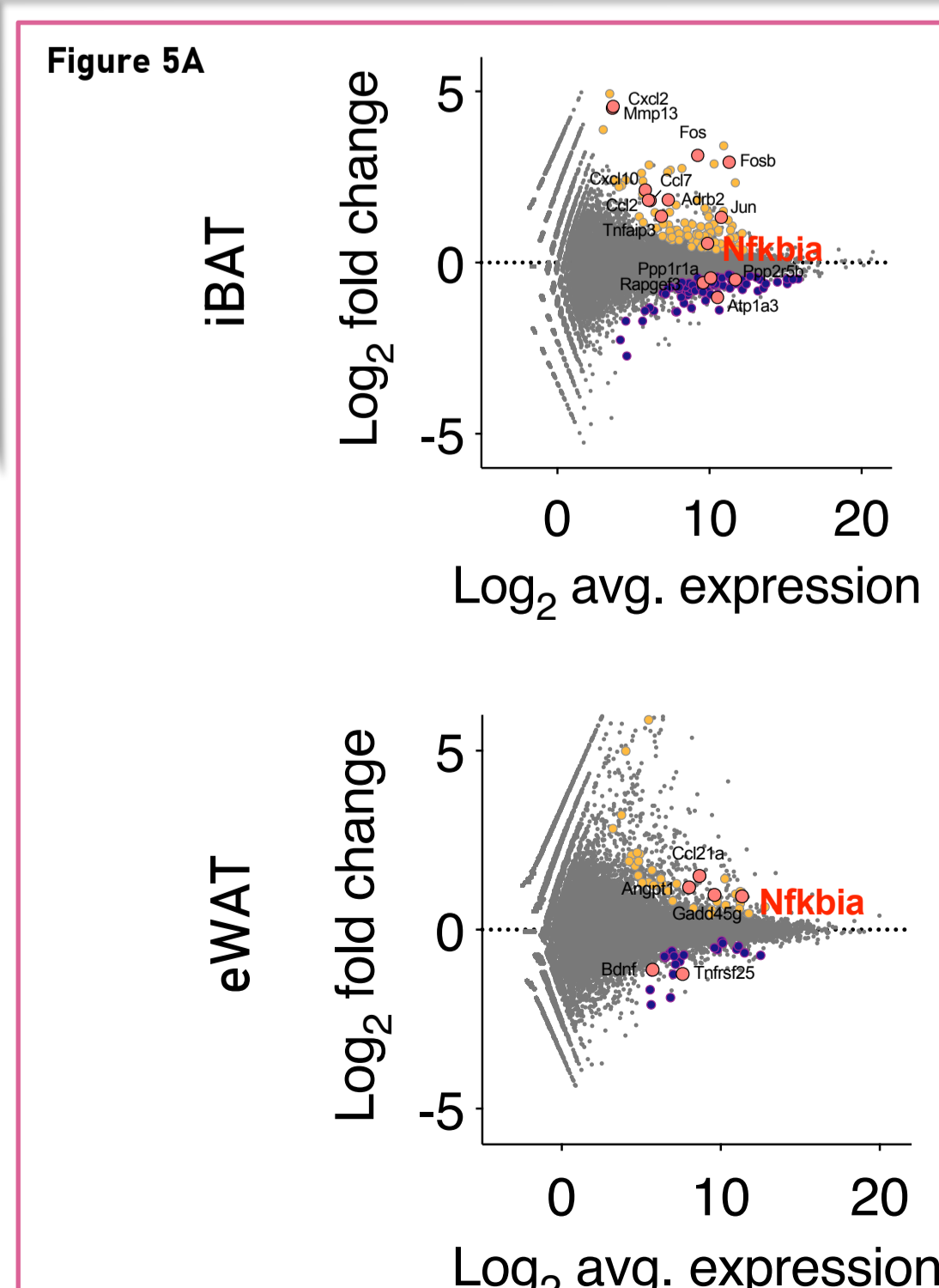


Figure 5: Inflammatory markers upregulation following POA PNOc neurons acute activation. A. Mean-difference plot of differentially expressed genes (padj) in interscapular brown adipose tissue (iBAT) and epididymal white adipose tissue (eWAT) one hour after POA PNOc neuronal activation. Tissues were collected one hour after CNO injection in PNOc-Cre and wildtype control animals. B. KEGG pathway analysis reveals inflammatory signatures in both iBAT and eWAT after POA PNOc neuron activation. C. Heatmap of upregulated genes in selected KEGG pathways after POA PNOc neuron activation.

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Summary: POA PNOc neurons intricately control energy expenditure through BAT thermogenesis and modulate inflammation in both BAT and WAT depots. Pharmacological targeting of these neurons could constitute a novel target for the treatment of obesity and diabetes.

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Declaration of interests: The authors declare no competing interests.

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