

SUPPLEMENTARY INFORMATION

Noradrenaline is a stress-associated metaplastic signal at GABA synapses

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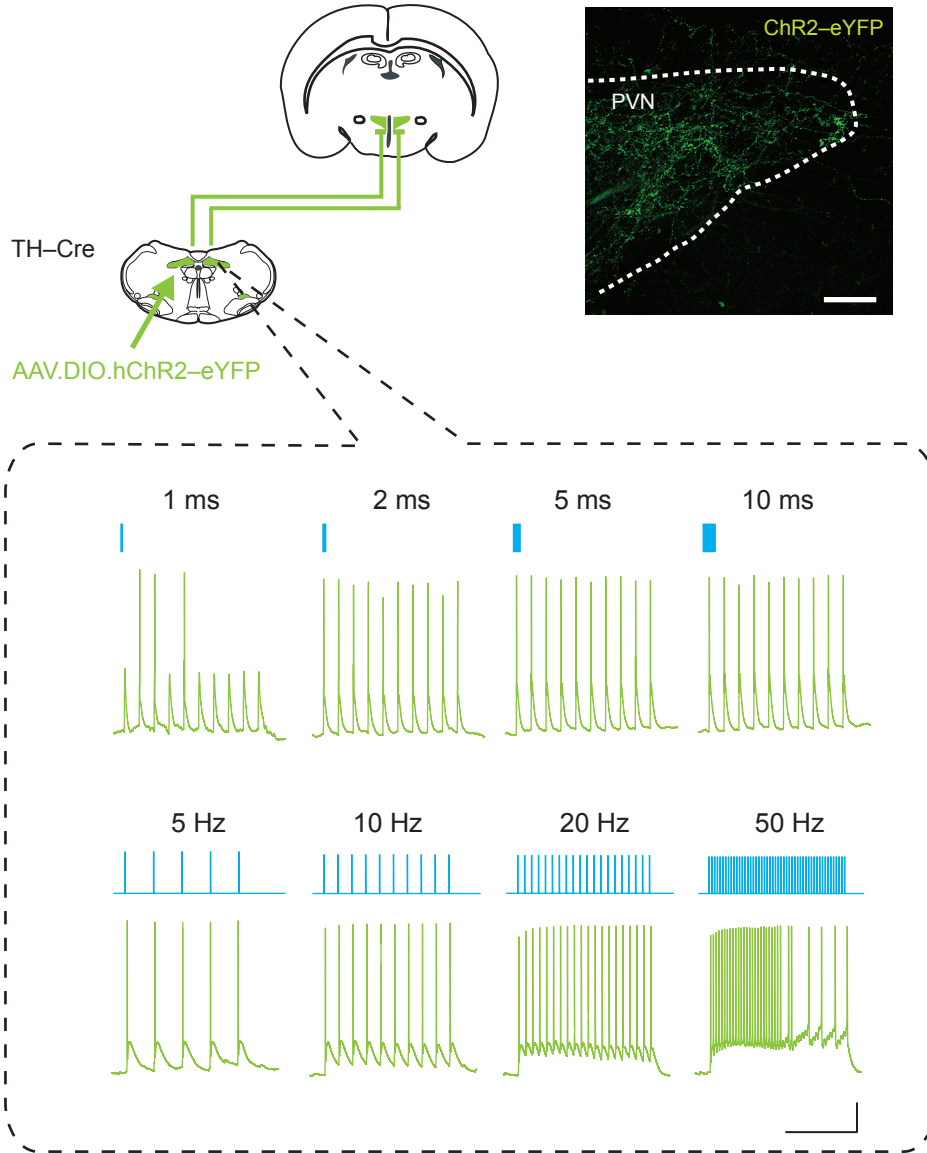
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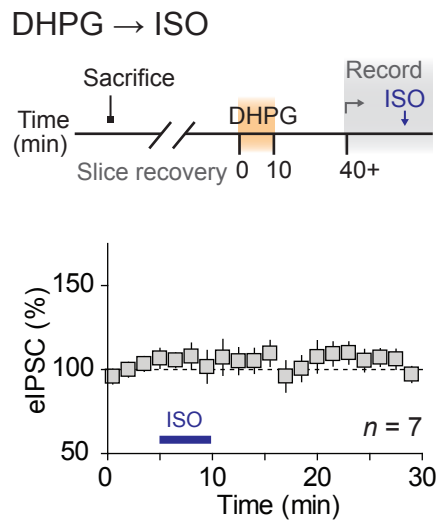
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Bains Supplementary Figure 1

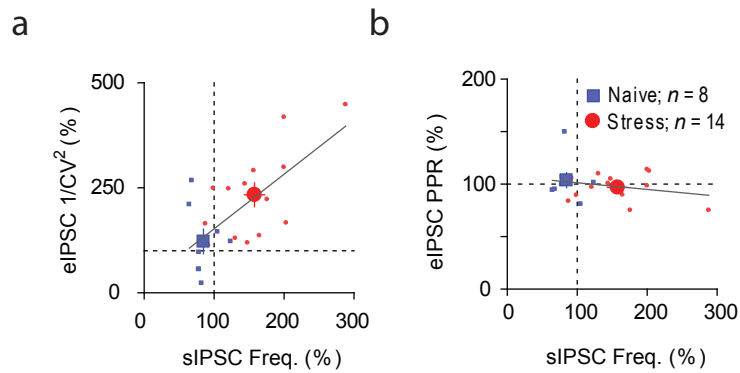


Supplementary Figure 1 Functional expression of ChR2. **Top left:** schematic for the strategy to deliver ChR2 gene expression in caudal medulla noradrenergic cells and in their terminals in the PVN. AAV.DIO.ChR2-eYFP is a recombinant adeno-associated viral vector (rAAV) with double floxed inverted open reading frame (DIO) construct carrying an inverted version of ChR2 fused to the fluorescent protein eYFP. In the absence of Cre recombinase, the coding region of ChR2-eYFP remains in antisense direction. In the presence of Cre, the transgene is flipped into the sense direction and expression of ChR2-eYFP can occur. AAV.DIO.ChR2-eYFP was stereotactically injected into the caudal medulla of TH-Cre mice. **Top right;** Expression of ChR2-eYFP terminals in the paraventricular nucleus (PVN). This representative image was taken from a histological experiment reproduced in three animals. Scale bar: 100 μ m. **Bottom:** Current clamp recording of neurons expressing ChR2-eYFP in brain stem slice (caudal medulla) in response to blue light pulse with variable durations (1-10 ms) and at variable frequencies (5-50 Hz, 5 ms pulse duration). Scale bars represent 0.5 s and 20 mV



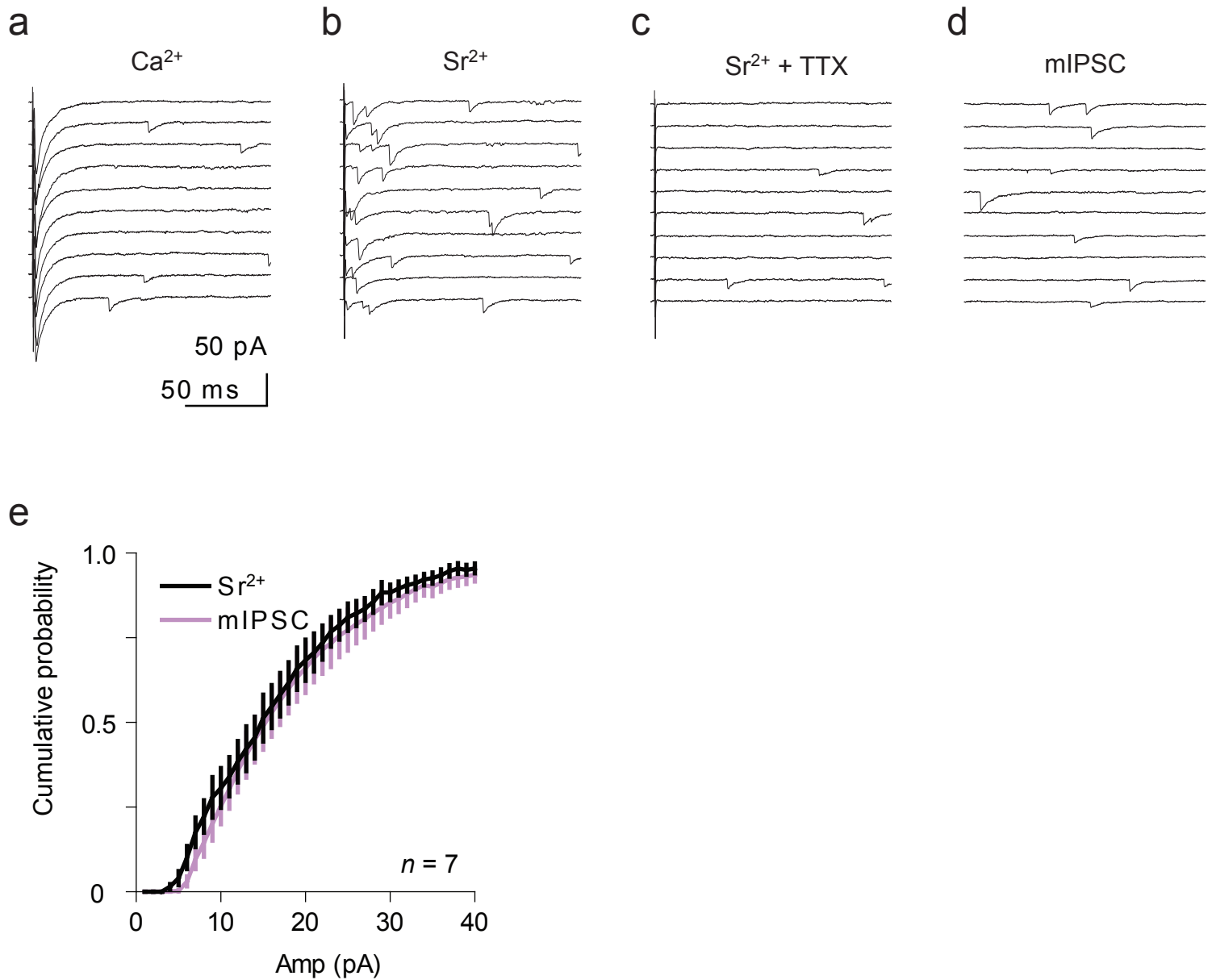
Supplementary Figure 2 MGluR1 → β -AR activation does not induce LTP_{GABA}. Left, schematics for the experiment. Bottom, summary time-course. Blue horizontal bar represents ISO application. Data are mean \pm s.e.m.

Bains Supplementary Figure 3



Supplementary Figure 3 Activity-dependent increase in sIPSC frequency is accompanied by changes in $1/CV^2$ but not PPR. **(a-b)** Plots of normalized $1/CV^2$ **(a)** and PPR **(b)** against sIPSC frequency after HFS, recorded in slices from naïve (blue) and IMO stressed (red) rats. Smaller circles and squares represent individual data and larger ones are their mean \pm s.e.m. Lines represent least square linear best fit (sIPSC frequency \times $1/CV^2$, $r = 0.7$, $p = 0.0007$; sIPSC frequency \times PPR, $r = 0.3$, $p = 0.3$).

Bains Supplementary Figure 4



Supplementary Figure 4 (a-d) Sample traces recorded sequentially from the same neuron. Replacing Ca^{2+} (a) with Sr^{2+} (b) in aCSF caused asynchronous small eIPSCs following presynaptic stimulation. (c) Asynchronous events are sensitive to TTX (1 μM). mIPSC observed in the absence of presynaptic stimulation (d). Cumulative amplitude distributions comparing evoked asynchronous eIPSC and mIPSC ($n = 7$).