

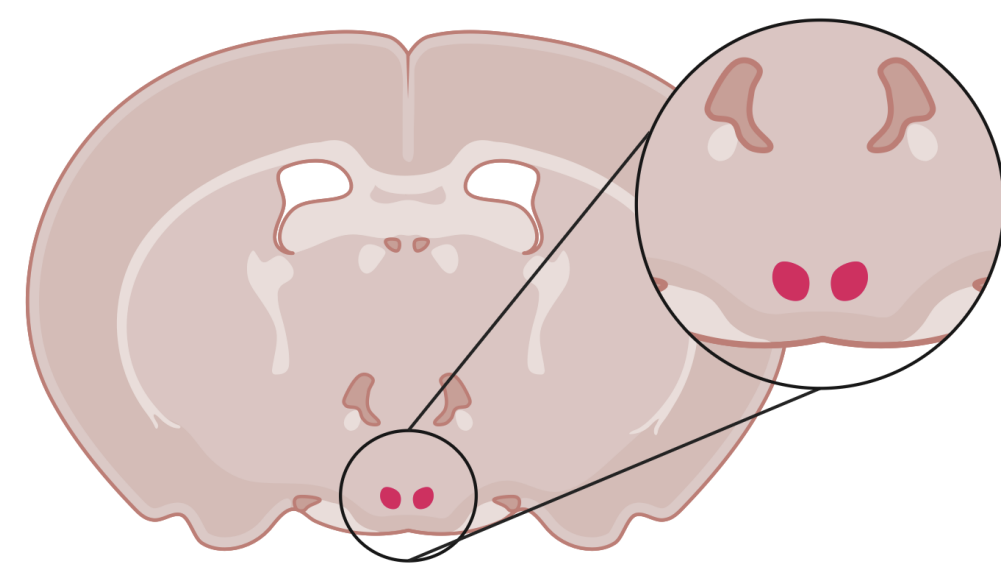
Acute Stress Decreases Glutamate Transmission in the Female Rat Dorsomedial Hypothalamus

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BACKGROUND

Stress response mechanisms have not adapted to our high stress society and landscape of high calorie, highly palatable foods¹. **Women** are particularly vulnerable to **disordered eating** behaviours when **stressed**², for which the neurophysiological basis is unclear. Yet, female research subjects remain underrepresented.

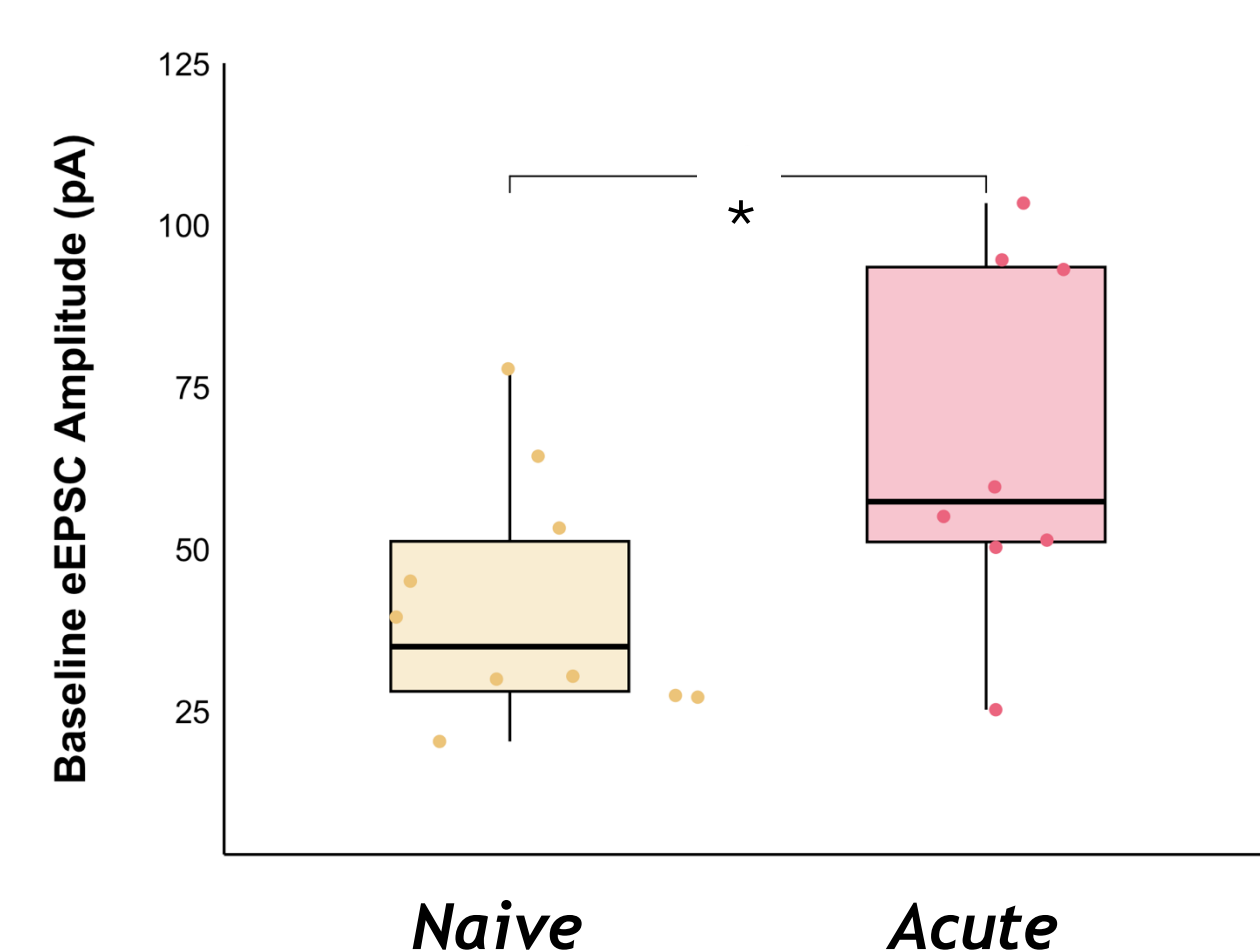


The **dorsomedial hypothalamus (DMH)** is a brain region involved in appetite and body weight regulation³, and the stress response⁴. Some DMH neurons increase appetite and have receptors for **stress hormones**⁵. How stress affects DMH neurons is unclear.

How **acute stress** in **females** affects **glutamatergic** transmission in the DMH is unknown.

RESULTS

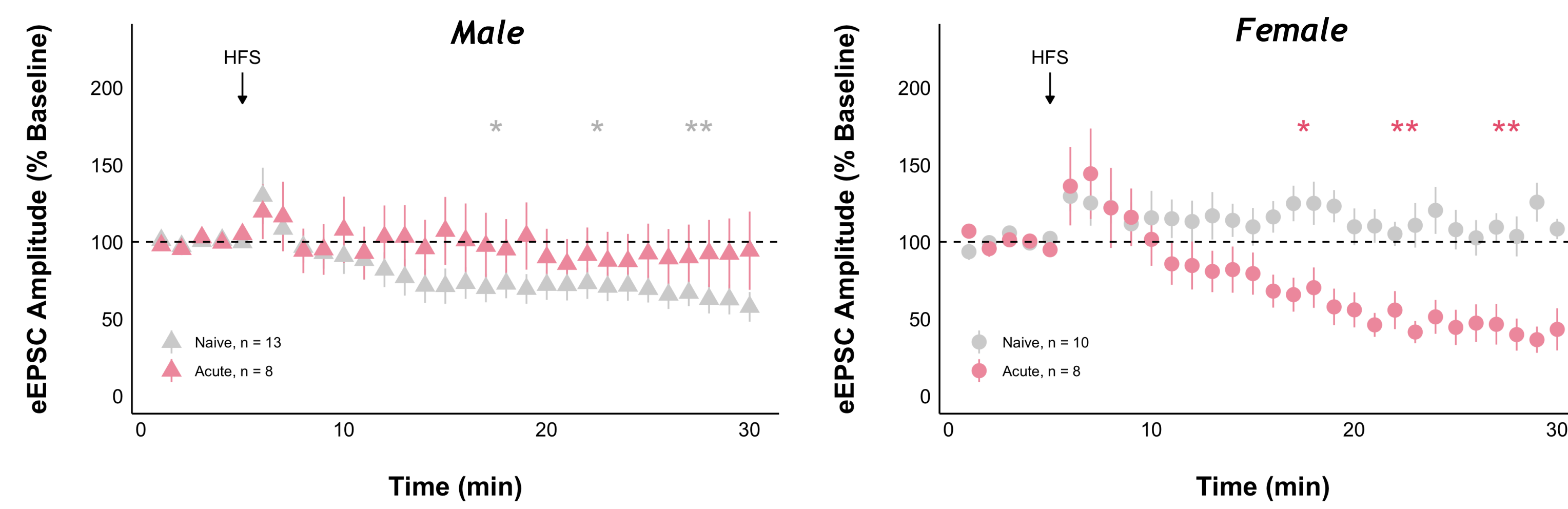
How does **acute stress** in **females** affect baseline glutamate transmission?



An unpaired *t*-test was used to compare between groups.
* = *p*-value < 0.05

There is a significant **increase** in eEPSC amplitude.

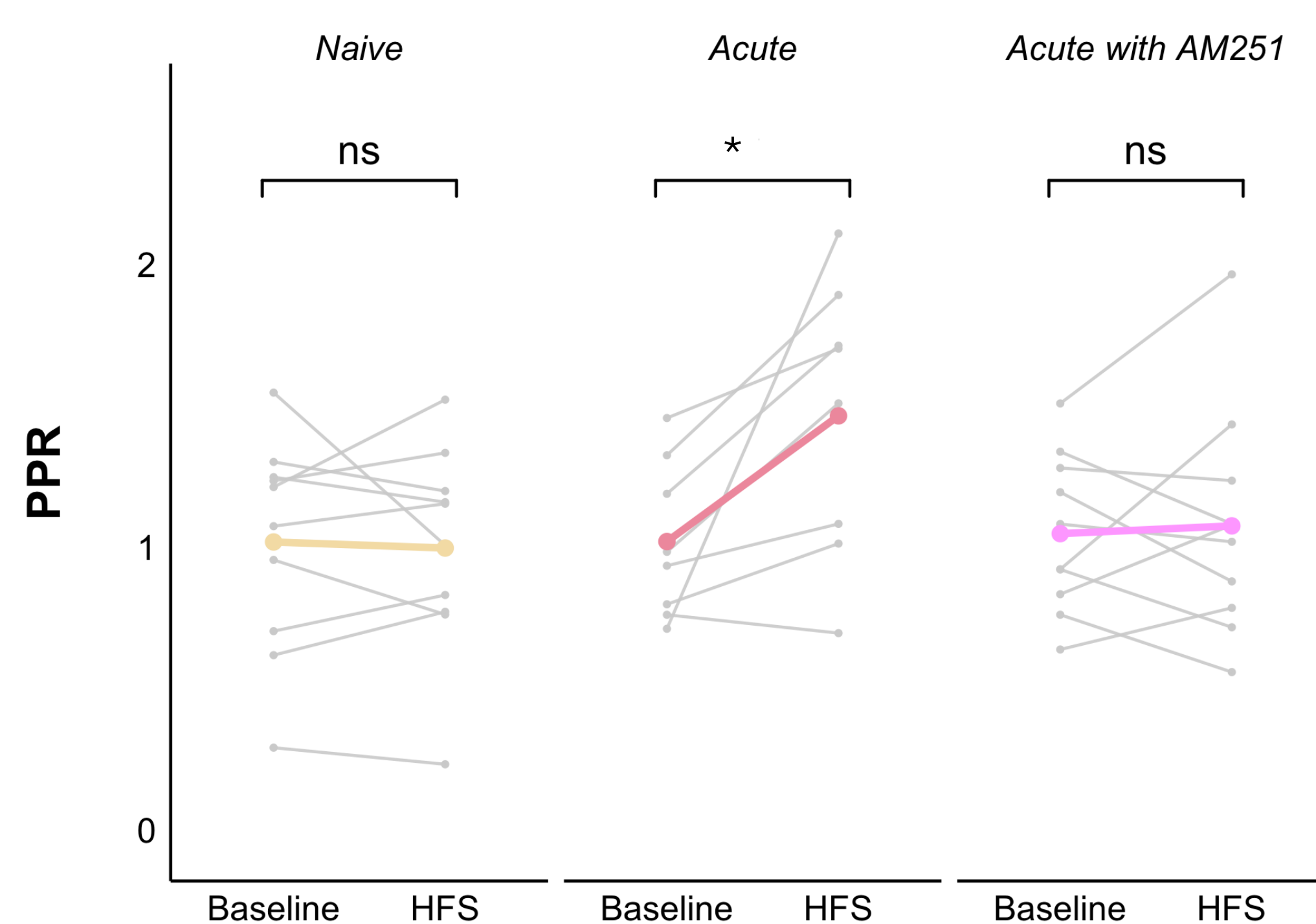
What about long term changes?



Naive female data collected by Lara Swart, male data collected by Sarah Wilson.
A paired *t*-test was used to compare each 5-minute interval to the 5-minute baseline period.
* = *p*-value < 0.05, ** = *p*-value < 0.01

Acute stress in **females** triggered a long-lasting depression in glutamate transmission compared to naive, but not in **males**.

Is the depression due to a presynaptic decrease in glutamate onto DMH neurons during **acute stress**?

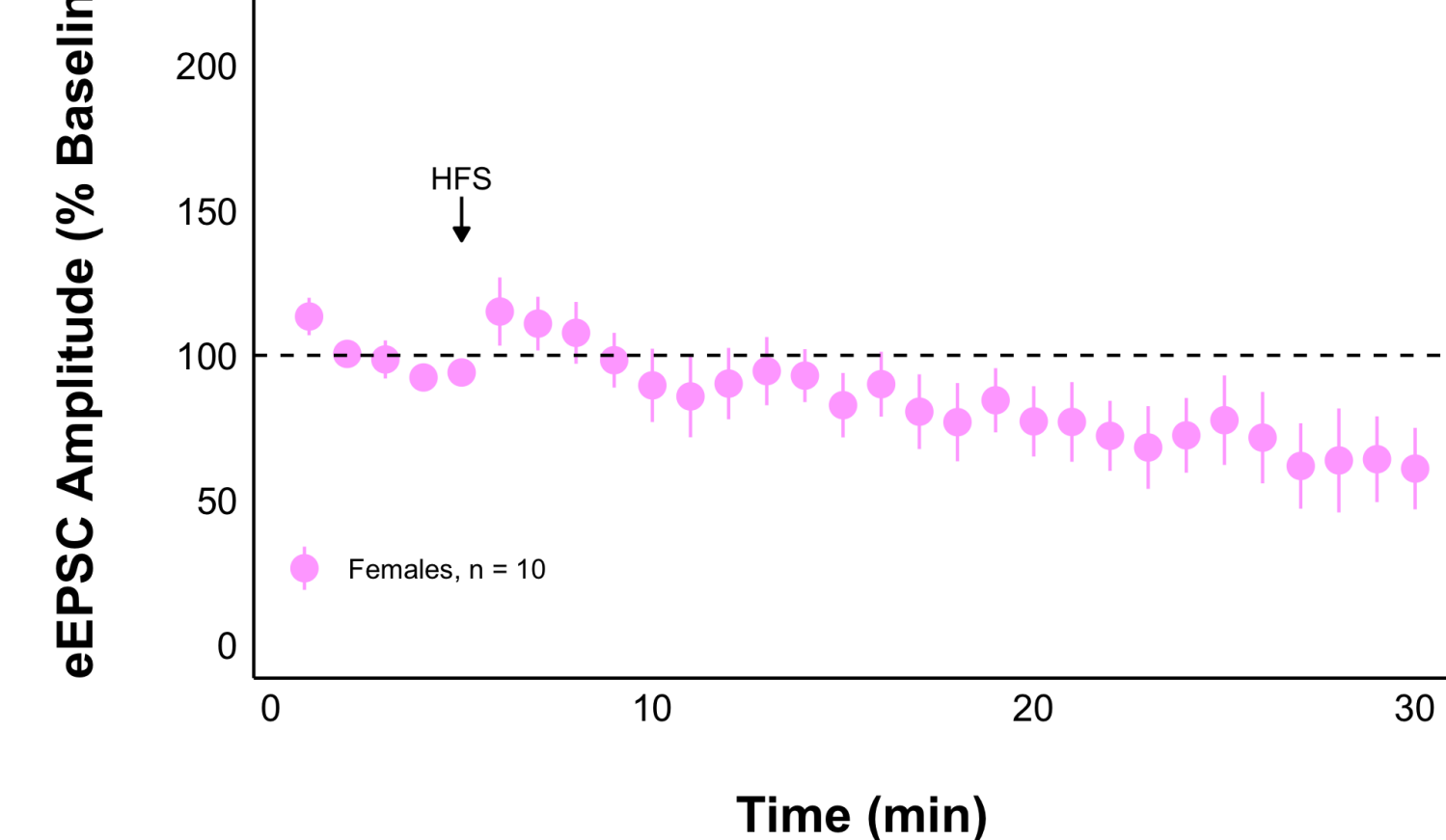


A paired *t*-test was used to compare between baseline and post HFS.
The PPR is calculated as the evoked current amplitude of peak 2/peak 1.

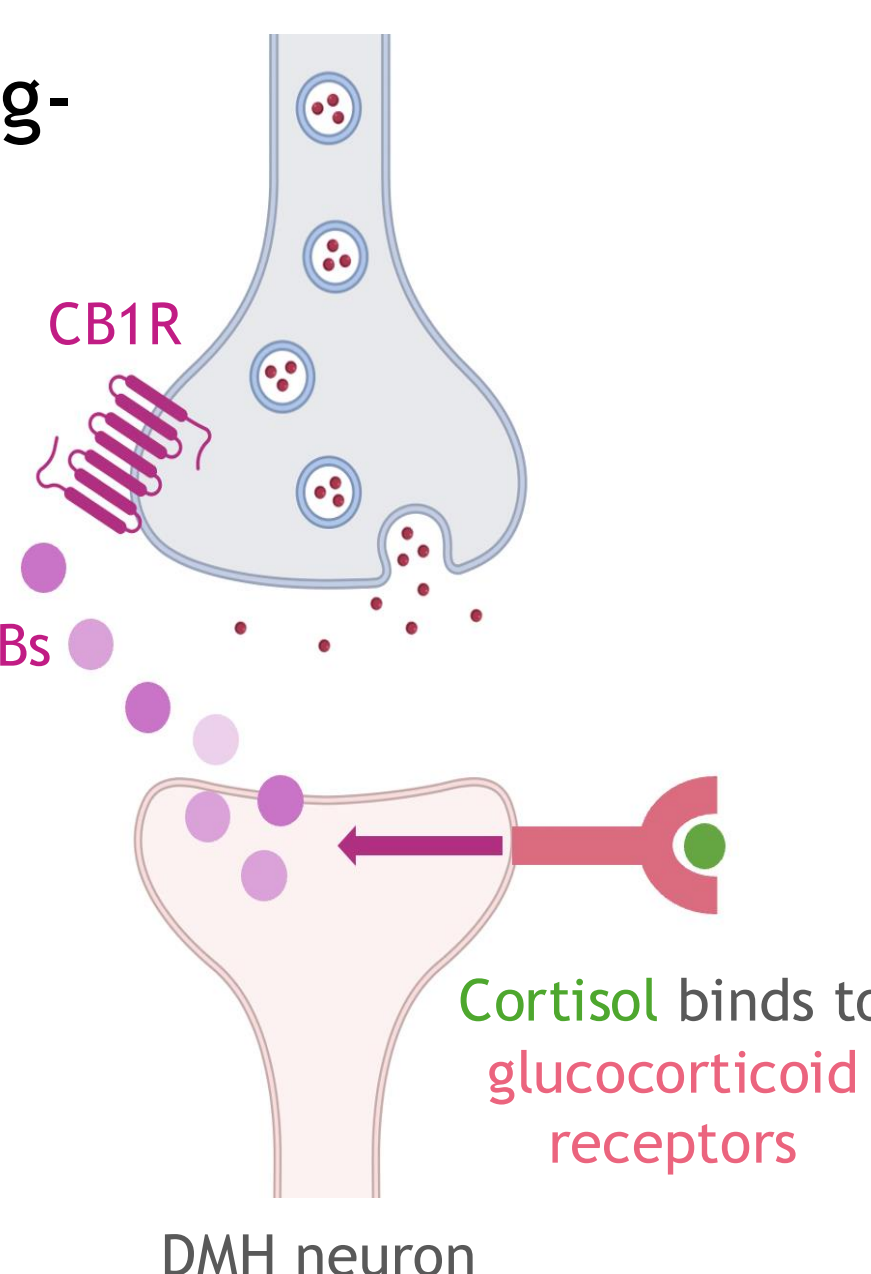
The PPR **significantly increased**, indicating a lower probability of glutamate release onto DMH neurons under **acute stress**, but there is no change in PPR when **eCB-CB1 receptors** are blocked under **acute stress**.

Endocannabinoids (eCBs) can trigger a long-lasting decrease in glutamate release.

AM251 blocks CB1 receptors (CB1R).
Acute Female with 5 μ M AM251



When **eCB-CB1 receptors** are blocked there is no longer a long-lasting decrease in glutamatergic current amplitude under **acute stress**.

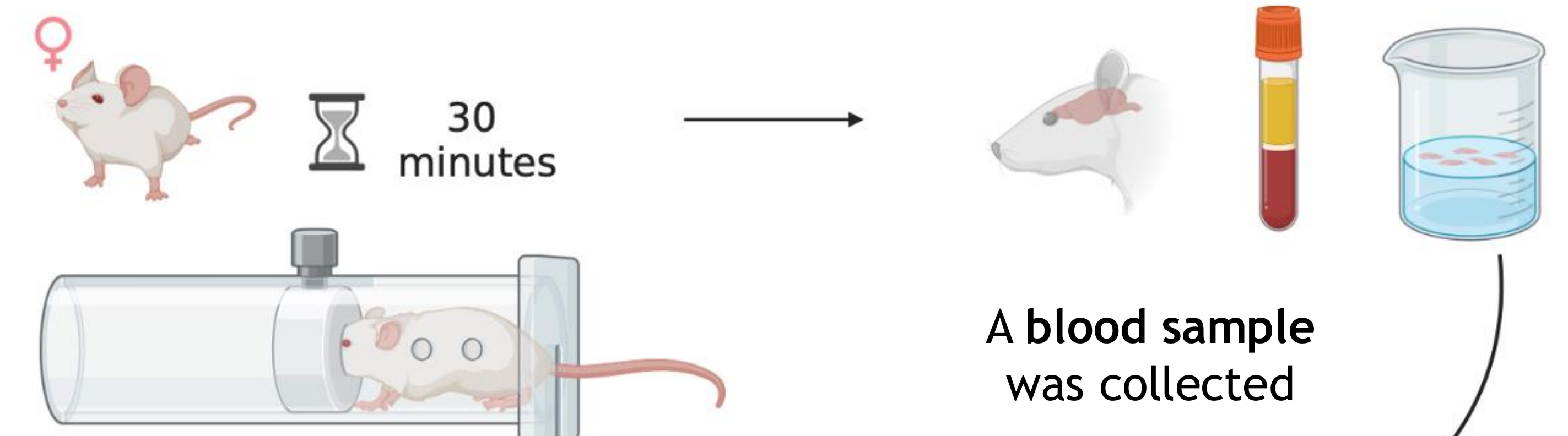


METHODS

Experiments were performed according to protocol #104140 approved by the Mount Allison University Animal Care Committee in accordance with the Canadian Council on Animal Care Guidelines

Young, **female** Sprague-Dawley rats were exposed to a single **restraint stress**

They were anesthetized, euthanized, and their **brains** were quickly removed

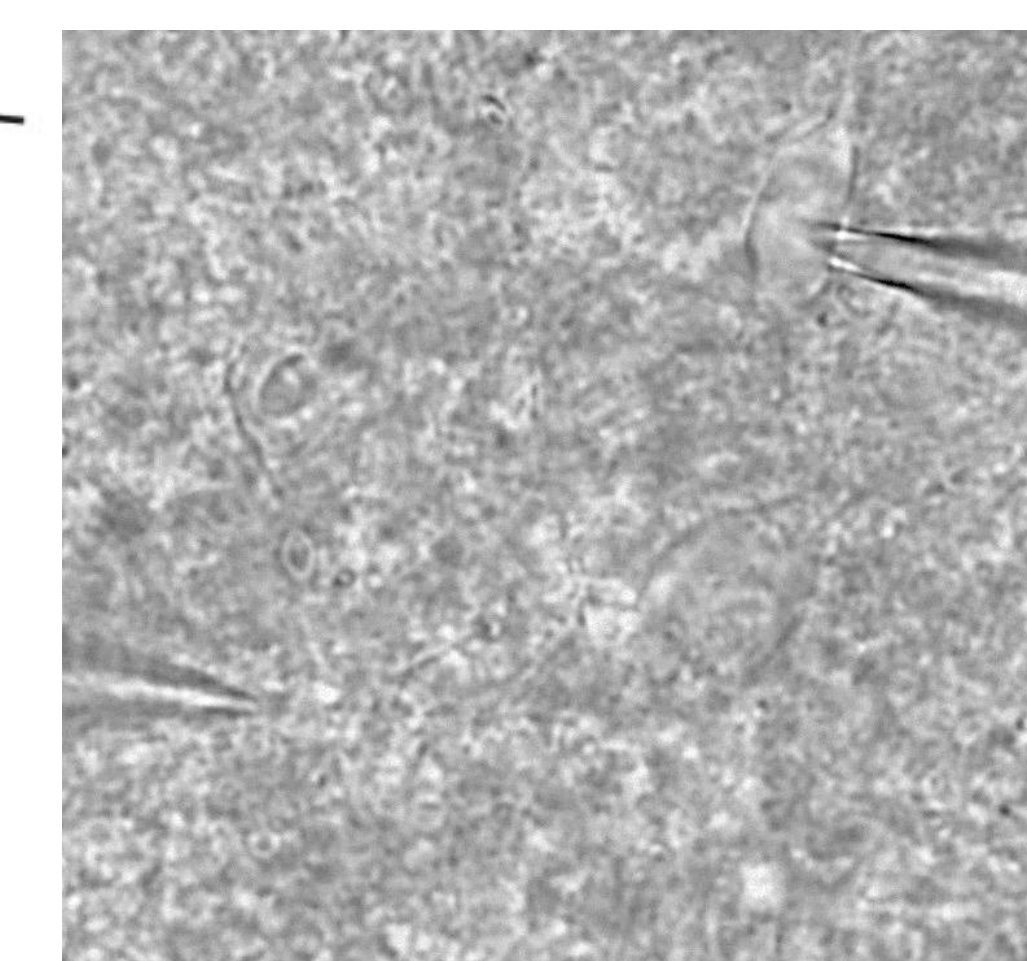


Recording electrode inserted into **DMH neurons**, and a stimulating electrode into surrounding tissue to evoke **excitatory postsynaptic currents (eEPSC)** at 0.2 Hz

Living neurons were recorded from before and after high frequency stimulation (HFS) to observe long-lasting changes

HFS Protocol: 100 Hz for 4 seconds, twice, 20 seconds apart

Data analysis was performed using patchclampplotter by Christelinda Laureijs⁶



250 μ m coronal brain slices containing the DMH were kept alive in oxygenated artificial cerebrospinal fluid kept at 32.5 $^{\circ}$ C

50 μ M picrotoxin was applied to observe **glutamate** synapses

CONCLUSIONS

- There are sex differences in glutamate transmission in the rat DMH.
- Females** who are **acutely stressed** have more glutamate transmission onto DMH.
- There is a long-lasting decrease in glutamate current amplitude and probability of presynaptic glutamate release under **acute stress**.
- The decreases in eEPSC amplitude and presynaptic glutamate release during **acute stress** are no longer significant when **endocannabinoid-CB1 receptors** are blocked.

FUTURE DIRECTIONS

Future work aims to determine:

- The effect of chronic (repeated) stress (**work in progress**) on the **female** rat DMH.
- How corticosterone is involved in the change in glutamate transmission under **acute stress**.
- The effect of stress on neuronal excitability.

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