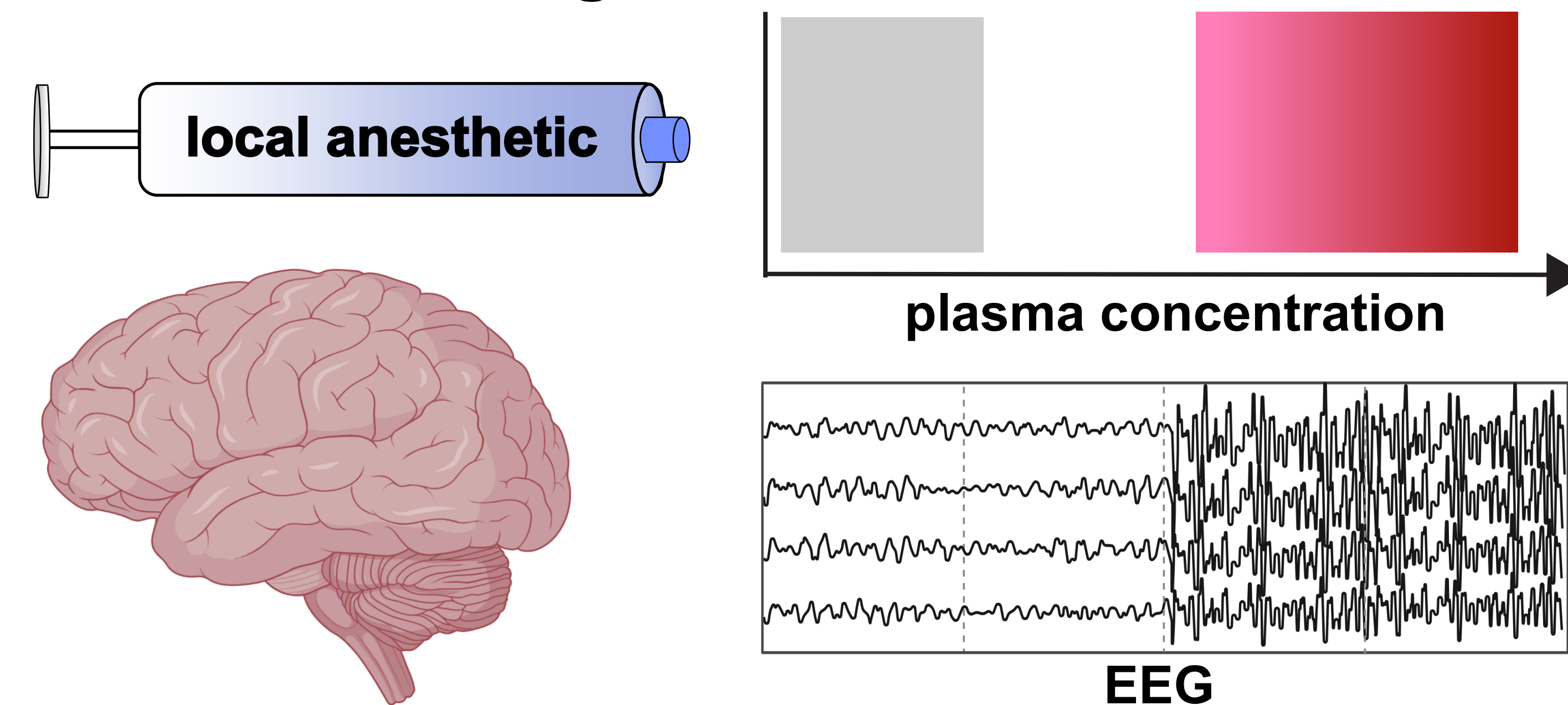


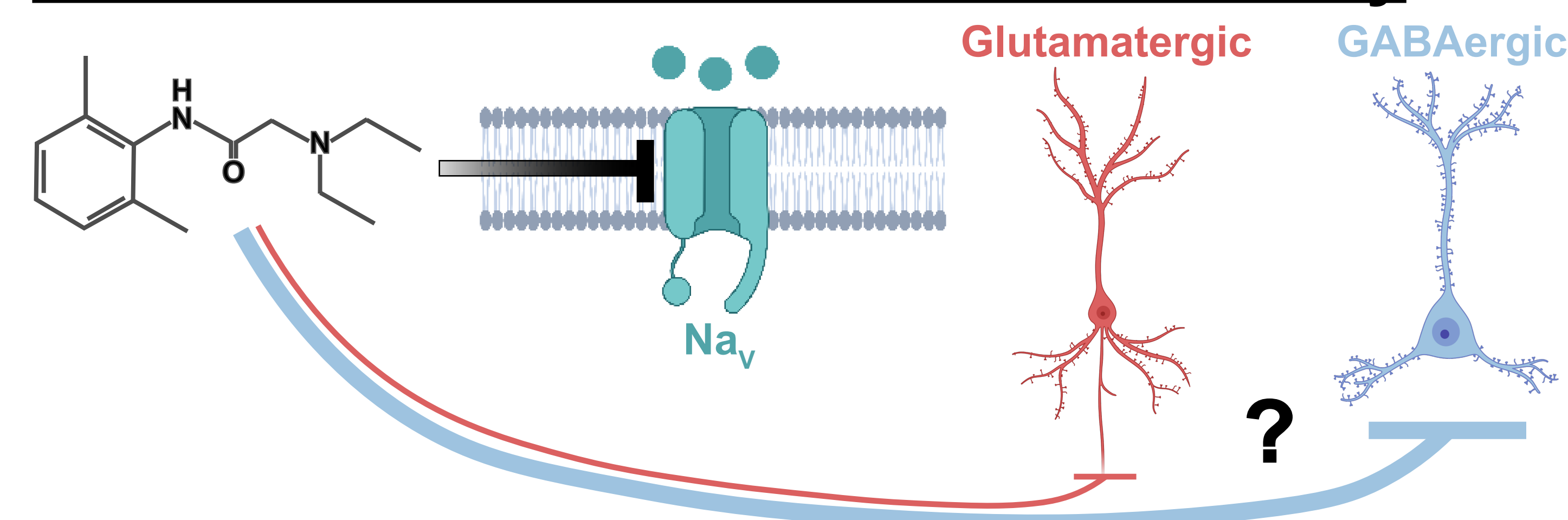
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Clinical Challenge



Local anesthetics are indispensable drugs for surgery and medical procedures. Intravascular overdose often leads to neurotoxicity, which can progress to seizures.¹

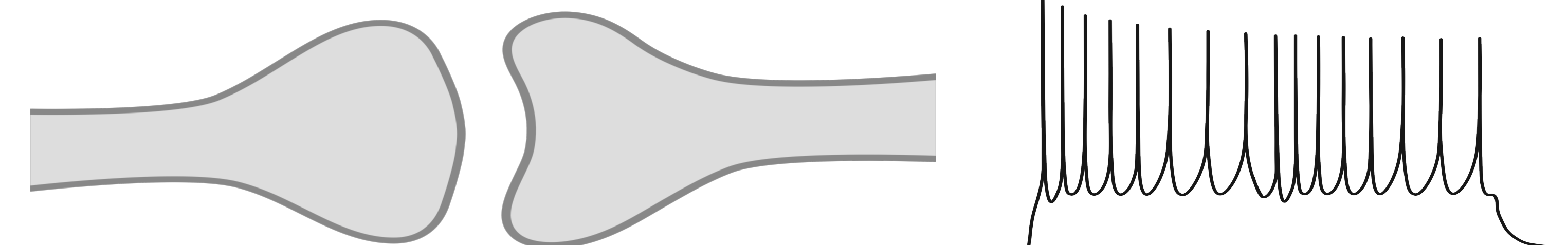
Models of local anesthetic neurotoxicity



Prevailing hypothesis is preferential targeting of inhibitory neurons²

May involve differential modulation of:

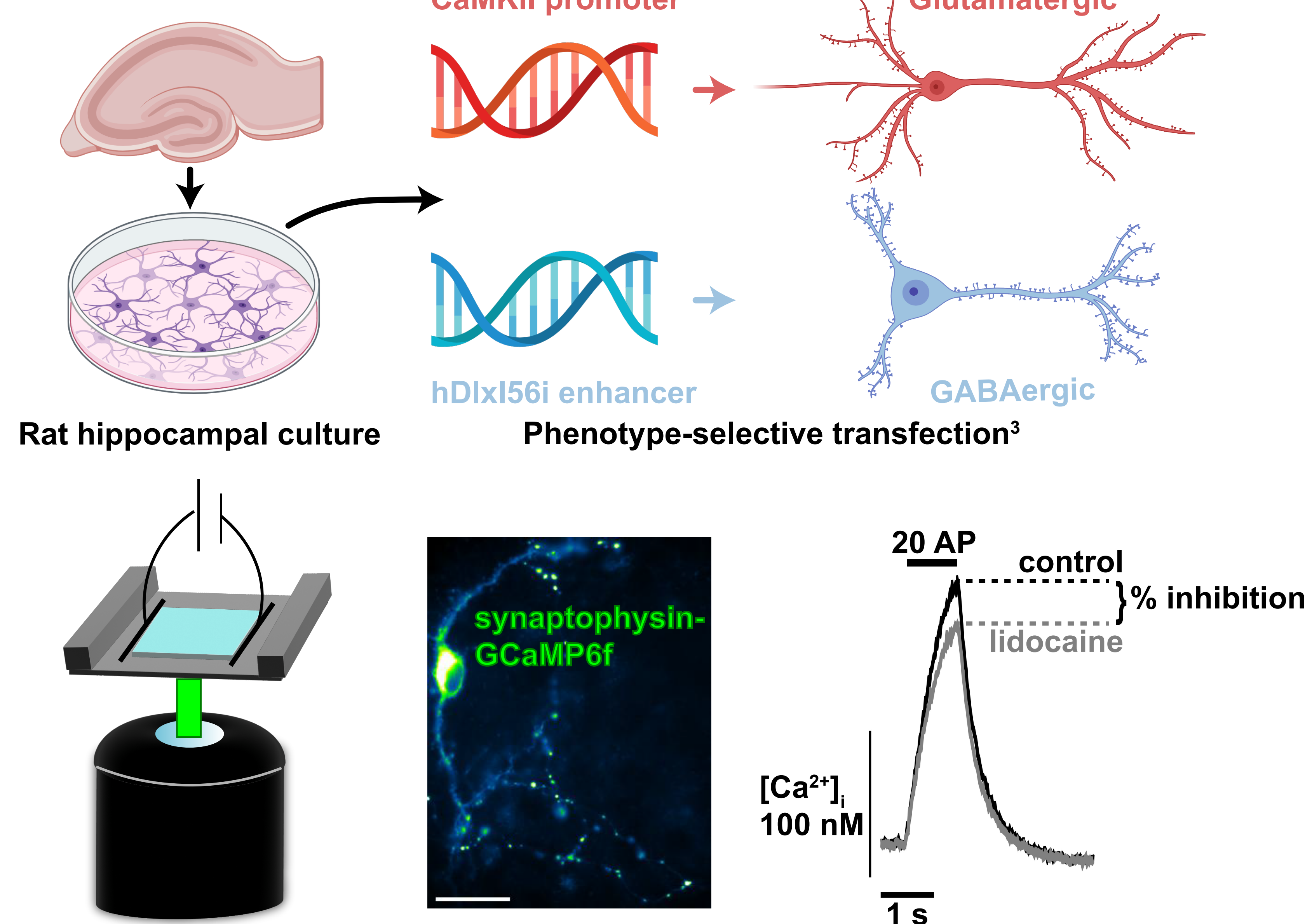
1. presynapse
2. postsynapse
3. excitability



Research Question

Does the prototypical local anesthetic, lidocaine, preferentially inhibit nerve terminals of GABAergic neurons compared to glutamatergic neurons?

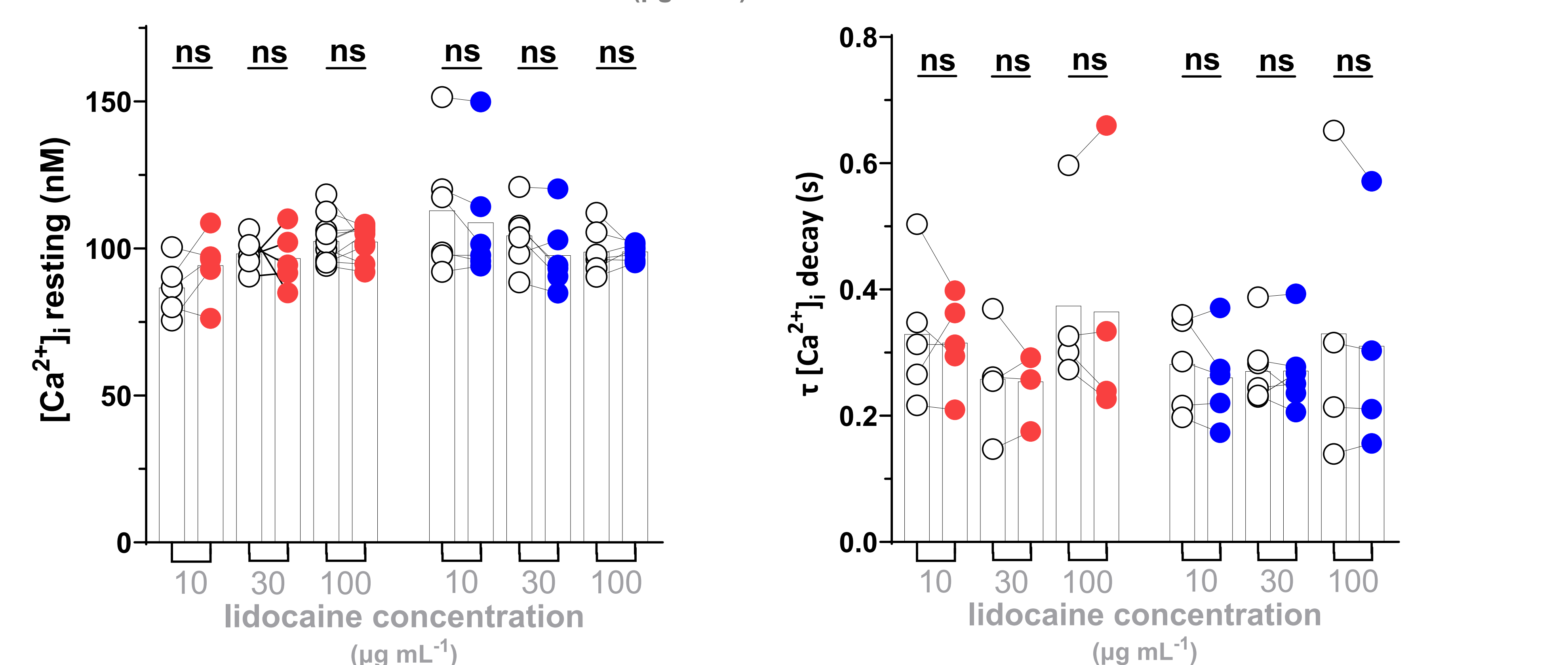
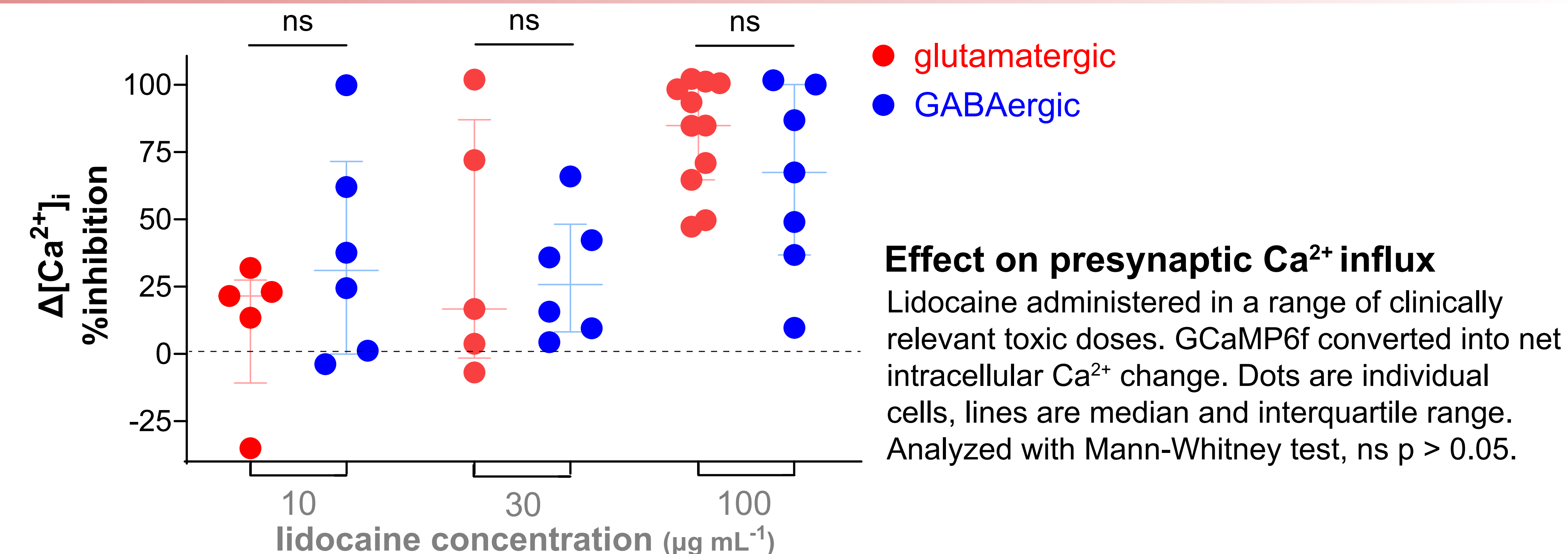
Methods



Fluorescence imaging of the genetically-encoded Ca²⁺ indicator, GCaMP6f, targeted to nerve terminals by synaptophysin and driven to fire action potentials (APs) by field depolarization. Lidocaine inhibition of synaptic function was quantified as the relative decrease of Ca²⁺ influx into nerve terminals compared to control. Scale bar = 20 μ m.

ACKNOWLEDGEMENTS

This research is supported by the National Institutes of Health (K08GM148935 to DCC; NS036942 and NS11739 to TAR). Figures were created with Biorender.com. Statistical analysis was performed with GraphPad Prism v10. We thank Giulia Dalaty for research technical support.



Secondary analysis: Effect on intracellular Ca²⁺ handling

Resting [Ca²⁺]_i and decay from peak after stimulation. Dots are individual cells, bars are mean. For decay data, cells with single exponential fit R² < 0.8 were excluded. Analyzed with paired t-test, ns p > 0.05.

Conclusions

Our results do not support preferential presynaptic inhibition of glutamatergic compared to GABAergic neurons. Future experiments will identify the molecular factors determining the unexpected variability of neuronal inhibition by lidocaine.

References

- 1) Di Gregorio et al. *Reg Anesth Pain Med*. 2010; 35:181-187.
- 2) El-Boghdady et al. *Local Reg Anesth*. 2018; 11:35-44.
- 3) Farrell et al. *bioRxiv* 2024.02.15.580492