

Introduction

Optogenetics offer both a powerful experimental tool among neurophysiological techniques and the promise of a therapeutic modality in greater clinical neuroscience. The ability to precisely target and modulate neuronal subpopulations finds particular use in understanding seizure genesis and propagation, one current area of rich investigation. Here, we investigate the role of bidirectional modulation of subpopulations of inhibitory cortical interneurons in a model of seizure activity.

Methods

Channelrhodopsin 2 (ChR2) and archaerhodopsin (ArchT) were expressed in murine parvalbumin- and somatostatin-expressing interneurons using Cre/lox selective recombination. Acute brain slices of the temporal neocortex were prepared and incubated in artificial cerebrospinal fluid. Standard patch clamp techniques were used to record from layer V cortical pyramidal cells and interneurons in whole-cell mode. Low-dose 4-aminopyridine (4-AP) was applied to lower the seizure threshold, and direct monopolar electrical stimulation was used to evoke an ictal event. A light source was utilized to concomitantly modulate

Results

In this model of evoked epileptiform activity, electrical stimulation in the presence of 4-AP elicited an epileptiform event 85% of attempts. Peri-stimulus activation of somatostatin-expressing inhibitory interneurons using ChR2 reduced the incidence of evoked seizures to 26%. Activation of parvalbumin-expressing inhibitory interneurons had no effect on the incidence of evoked ictal events (89%). There was no statistical difference in the inhibitory post-synaptic current delivered to cortical pyramidal cells between the somatostatin-ChR2 (1391 pA) and parvalbumin-ChR2 (1900 pA) cohorts ($p=0.216$). However, peri-stimulus inhibition of parvalbumin-expressing interneurons with ArchT-mediated currents lead to a significant reduction in evoked epileptiform events (33%)

Conclusions

Optogenetic activation of somatostatin-expressing but not parvalbumin-expressing cortical interneurons impedes ictogenesis in an in vitro model of seizure activity. The net inhibitory charge delivered to cortical pyramidal neurons does not account for this differential effect. Paradoxically, inhibition of parvalbumin-expressing inhibitory interneurons substantially decreases the probability of evoking an ictal event. Taken together, these findings suggest differential roles for inhibitory interneurons in seizure generation or propagation, and a further understanding of these phenomena may offer points of therapeutic intervention.

Learning Objectives

To understand the differential effect of optogenetic modulation of interneuron populations on ictogenesis

References

- Paz JT and Huguenard JR. 2015. Optogenetics and Epilepsy: Past, Present, and Future. *Epilepsy Currents*. Vol 15. No 1.
- Sessolo M, et al. 2015. Parvalbumin-positive inhibitory interneurons oppose propagation but favor generation of focal epileptiform activity

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