Effects of Trigeminal Nerve Stimulation on Neuron Firing and Local Field Potentials in the Neocortex of Awake Rats

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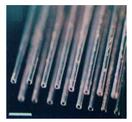
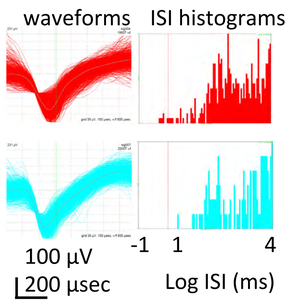
Abstract

Trigeminal nerve stimulation has been shown to reduce seizure activity in animal models of epilepsy and humans. However, the mechanism(s) by which this occurs is unknown. A fundamental question is: How do neurons in the somatosensory neocortex respond to the high frequency trigeminal stimulation that has been shown to be necessary for the anti-seizure effect? In this study, we recorded from multiple single neurons simultaneously in the primary somatosensory cortex of awake rats using arrays of chronically implanted microwire electrodes. We also implanted a nerve cuff electrode on the infraorbital branch of the trigeminal nerve contralateral to the recording site. Unimodal pulses were provided to the infraorbital nerve with current values ranging from 1-9 mA and at frequencies of 1-100 Hz. Trigeminal nerve stimulation reduced the firing of single neurons in a frequency-dependent manner, with maximal firing reduction at frequencies of 62.5 Hz and above. This effect was not greatly dependent on stimulus intensity throughout the current range tested. Each pulse to the infraorbital nerve was followed by a short latency (approximately 7 ms) response, followed by a period of post-stimulus inhibition. These results suggest that therapeutic levels of trigeminal nerve stimulation may exert their effect in part by suppressing neuronal firing using intrinsic cortical inhibitory mechanisms.

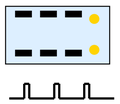
Methods



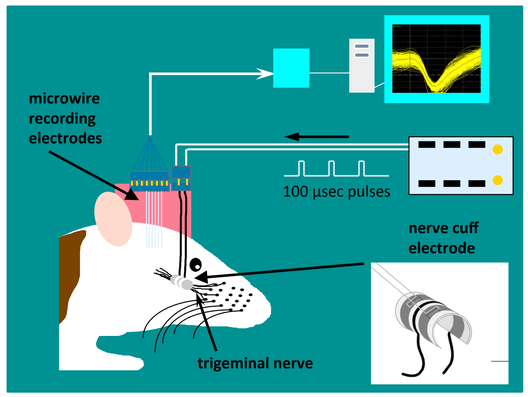
Multi-electrode arrays (MEAs):
- 25-50 micron diameter platinum or stainless steel wires
- 8 x 2 arrays
- Chronically implanted into layer 5 of primary somatosensory cortex (SI) of female Long-Evans hooded rats (-3.0 RC, 5.5 ML)



Stimulating cuff electrode:
- Two bands of platinum foil
- Outside coated with Sylgard
- Implanted around infraorbital branch of the trigeminal nerve (V_2) contralateral to MEA



Stimulus parameters:
- 1-9 mA current amplitude
- 1-120 Hz stimulation frequency
- Monophasic 500 microsecond pulses

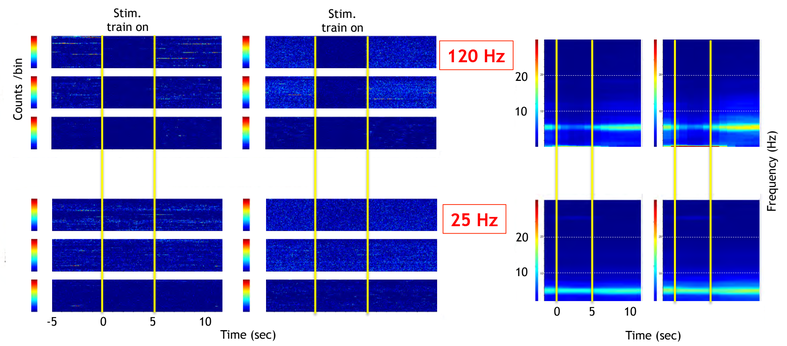


Recording parameters

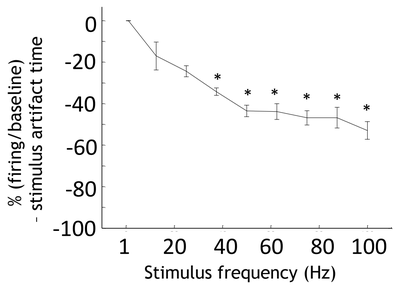
	Single and multi units	Local field potential
Filtering Low cutoff	154 Hz	0.7 Hz
Filtering High cutoff	8.8 kHz	300 Hz
Sampling rate	40 kHz	1 kHz
Gain	variable	5-10 k

Results

TNS reduces neuronal firing and LFP theta frequencies

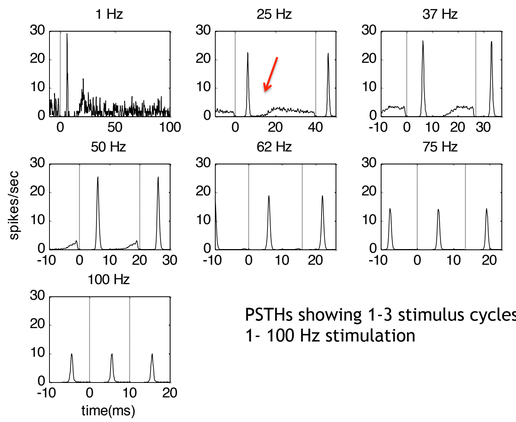


Quantification of firing reduction



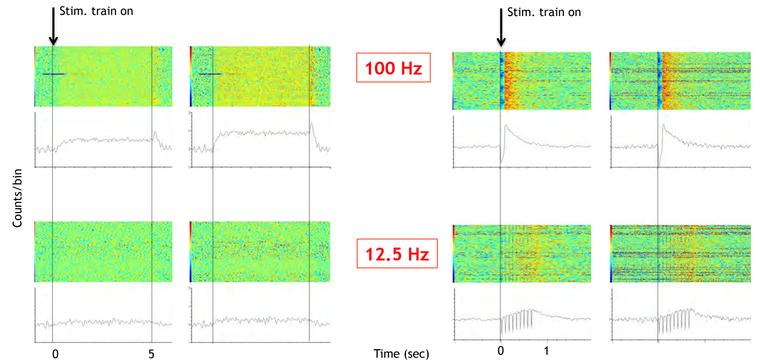
Firing during stimulus, relative to background firing rates for each neuron. Stimulus artifact periods subtracted. ANOVA $p < 1 * 10^{-5}$; * indicates $p < 0.05$ in Bonferroni post-hoc tests.

Post-stimulus inhibition influences firing during trigeminal nerve stimulation



PSTHs showing 1-3 stimulus cycles for 1- 100 Hz stimulation

TNS alters local field potential signals during and after stimulus trains



Conclusions

- Neocortical excitatory neuron firing is reduced in a frequency-dependent manner during trigeminal nerve stimulation
- This effect may be mediated in part by the post-stimulus inhibition period following the initial sensory response to trigeminal stimulation
- TNS alters local field potential signals both during and for some time after the stimulus trains

References

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Acknowledgements

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