Translational Neuroscience Case Study

A two tier approach to investigate compound activity on cortical neurons

Stage 1: Microelectrode array recordings (MEA): Rat cortical neurons

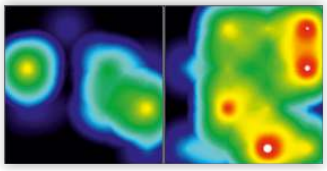
Neuronal activity substantially reduced by frequency-dependent sodium channel (Na_v) blocker.

- Axion Maestro MEA recording system used; 768 electrodes; 48 wells; 16 electrodes per well.
- Rat cortical neurons cultured for 3 weeks; activity monitored throughout; activity stable after ~2 weeks.
- General activity, burst behaviour & synchronization examined.

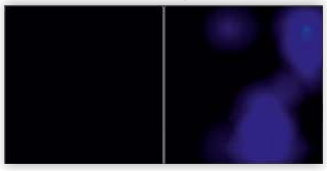
Axion Maestro Platform & 48 well plate

Activity heatmaps (2 representative wells)

Control

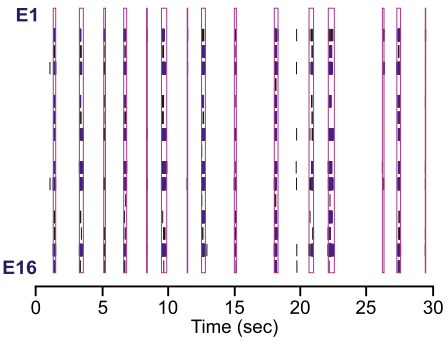


Drug

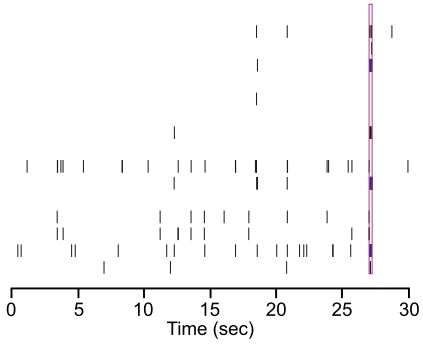


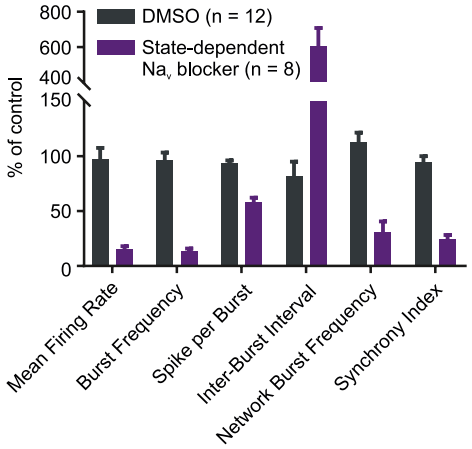
Raster plots of bursting behaviour in example well (16 electrodes)

Control – synchronized bursting



Drug – little synchrony

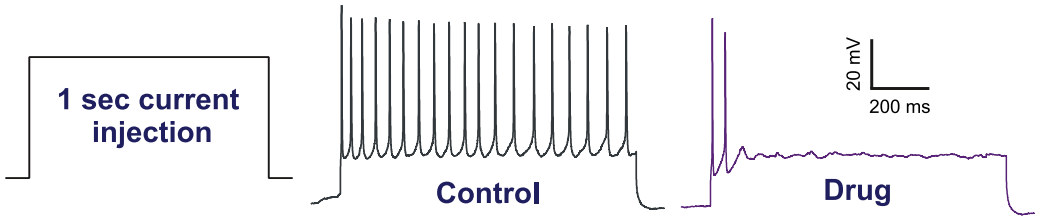


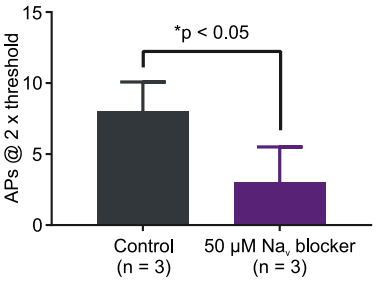


- Frequency-dependent Na_v blocker reduced spontaneous firing, burst frequency & spikes per burst.
- Network bursting decreased & synchronization of bursting reduced.
- Assay allows investigation of multiple compounds / concentrations on neuronal firing behaviour.

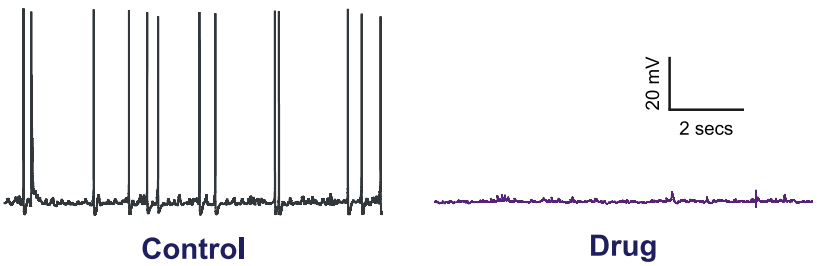
Stage 2: Manual patch current-clamp recordings: Rat cortical neurons

Evoked action potential train is truncated by frequency-dependent sodium channel blocker





Spontaneous action potentials are inhibited by frequency-dependent sodium channel blocker



- Evoked & spontaneous action potentials inhibited by Na_v blocker.
- Resting membrane potential & input resistance not significantly changed, ruling out alterations in passive membrane properties as the cause of the effects.
- Rat cortical neuron patch clamp assay stable & sensitive to expected drug effects.
- Assay allows investigation of compound effects on firing behaviour, validating mechanisms-of-action.

www.metrionbiosciences.com
info@metrionbiosciences.com

metrion biosciences