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An increased N-methyl-D-aspartate receptor conductance is associated with intrinsic bursting behavior

Amber Martell*[1], Seoan Marler[1], Hyong C Lee[1], Jan-Marino Ramirez[2] and Wim van Drongelen[1]

Address: [1]Department of Pediatrics, University of Chicago Hospitals, The University of Chicago, Chicago, IL, USA and [2]Department of Organismal Biology and Anatomy, The University of Chicago, Chicago, IL, USA

Email: Amber Martell* - martella@uchicago.edu

* Corresponding author

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Background

Seizure activity is often accompanied by an increase in the number of intrinsically bursting neurons [1]. The N-methyl-D-aspartate (NMDA) receptor, a channel known to be involved in many seizure models, represents one mechanism by which intrinsic bursting may arise, since 30–50% of these channels are bound at ambient concentrations of glutamate. In adult rat, intrinsic bursting has been induced in pyramidal neurons of the prefrontal cortex (PFC) through a combination of NMDA and dopamine type 1 (D1) receptor agonist [2]. Here we used the in vitro mouse neocortex and a computational model to further investigate the basis for bursting in the context of epileptiform activity.

Results

In mouse frontal cortex, application of 8–10 μM NMDA and 2–5 μM D1 agonist SKF 38393 elicited intrinsic bursting in ~50% of pyramidal neurons. A computational pyramidal neuron model consisting of five compartments with the sodium, potassium, calcium-activated potassium and NMDA channels was used to investigate the conditions necessary for bursting. In this model D1 agonist caused an amplification of the NMDA current. Our simulations indicate that increasing the NMDA receptor conductance transformed a regularly spiking neuron into a burster (see fig. 1). Interestingly, the bursting behavior

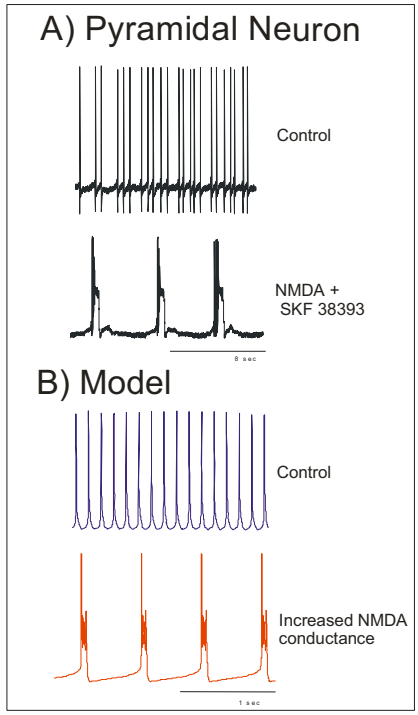

Figure 1
Experimental and Model Neuron Firing Behaviour.

appeared only when both NMDA receptor and calcium-activated potassium conductance were included.

Conclusion

The NMDA receptor is associated with production of intrinsic bursting behavior in mouse cortical pyramidal neurons, and, together with a calcium-activated K conductance, is sufficient to cause spontaneous bursting in a computational model of pyramidal neuron. These and previous results indicate that the NMDA receptor has the potential to drive the bursting behavior that characterizes seizures.

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