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Neuronal desynchronization may act as a trigger for seizure generation

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Background

Experimental reports have appeared which challenge the dogma that epileptic seizures arise as a consequence of neuronal hypersynchronization. We sought to explore what mechanisms that desynchronize neuronal firing could induce epileptic seizures.

Methods

We constructed a computer model of the neuronal network in the CA3 region of hippocampus, a region in the brain frequently associated with seizure generation. The model incorporates two distinct inhibitory hippocampal feedback circuits that have recently been reported [1]. Selective changes in the distribution of interneurons in the hippocampus of patients with epilepsy have also been reported [2,3]. Such changes could result in pathological alteration to synchronization of excitable cells with a potential causative role in epilepsy.

Results

When inhibition by interneurons that synapse on pyramidal dendrites was decreased, highly localized seizure-like bursting was observed in the CA3 region similar to that which occurs experimentally under GABAergic blockade. In contrast, when interneurons that synapse in the axo-somatic region were similarly decreased, no such bursting was observed. However, when this transient inhibition was increased, normal coordinated spread of excitation was interrupted by high frequency localized seizure-like bursting. The increase of this inhibitory input resulted in decreased cell coupling of pyramidal neurons. A decrease in phase coherence was initially observed until seizure-like activity initiated causing a net increase in coherence as has been observed in epileptic patients.

Conclusion

In addition to producing electrical behavior consistent with other models of epileptogenesis, our results indicate how preservation or relative augmentation of a particular inhibitory circuit could produce initial desynchronization ultimately initiating neuronal activity characteristic of partial seizures in which the aberrant electrical activity originates from and remains restricted to a limited region of the brain. Our analysis of these results also resolved conflicts in previously reported experimental results between brain slice and *in vivo* recordings of epileptiform activity. These results provide a possible pathway in which a decrease in synchronization could provide the trigger for inducing epileptiform activity.

References

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