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Effect of experimental Epilepsy on inhibition of GABAergic interneurons: Implications for comorbidities and therapeutic failures

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Strong perisomatic inhibition by Fast-Spiking Basket Cells (FS-BCs) and two classes of Accommodating Interneurons (AC-INs) regulate propagation of activity through the hippocampal dentate gyrus. Activity patterns of these interneurons are in turn governed by homotypic connections between similar neurons and heterotypic inhibitory inputs from other inter-neuronal classes. We have examined whether inhibitory control of dentate FS-BC and AC-INs is altered in experimental epilepsy. We find that pilocarpine-induced status epilepticus leads to functional changes in synapses from AC-INs to FS-BCs and strengthening of synapses between AC-INs. However, characteristics of synapses from FS-BCs remain unaltered. Additionally, we find cell-type specific changes in extra synaptic inhibition of FS-BCs following seizure induction. Thus, the nature of the perisomatic inhibitory network is altered after seizures. In computational simulations, the experimentally identified changes in inter-neuronal inhibition compromise network oscillations proposed to underlie memory function. Implication of the observed changes to memory dysfunction and therapeutic failures in epilepsy will be discussed.

Biography

Viji Santhakumar completed her MD in India and PhD from the University of California at Irvine. Following successive Postdoctoral studies at UCLA, she joined NJMS as an Assistant Professor in 2008 and was promoted to Associate Professor in 2014. Her lab exploits physiological and computational techniques to study inhibitory and neuro-immune plasticity in epilepsy and brain injury. She has over 20 peer-reviewed publications in leading journals and heads a vibrant research group with active collaborations.

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