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Presentation Abstract

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Presentation Title:	Asynchronous release of GABA reduces network gamma activity in a model of schizophrenia based on downregulation of parvalbumin at inhibitory synapses
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Abstract:	Psychiatric illnesses such as schizophrenia are often associated with alterations of neural oscillations in gamma (30-80 Hz) range. Deficits in gamma activity correlate with the reduced expression of parvalbumin in fast-spiking interneurons. Parvalbumin might modify the release of GABA from the synaptic boutons of interneurons by an unknown mechanism. The present study had two objectives: 1) to explore how synaptic plasticity (in particular synaptic depression) at GABAergic synaptic terminals of fast-spiking interneurons affects the observed network gamma rhythms; 2) to investigate the implications of deficits in synaptic parvalbumin on synchronization of neurotransmitter release and emergent gamma rhythms. To achieve these objectives, a biophysically realistic computational model of 2D cortical network was developed comprised of 900 (30x30) pyramidal neurons and interneurons (PY/IN ratio 4:1) organized in a 2D square lattice with locally random synaptic connectivity. Synaptic plasticity of multiple modes of transmitter release (phasic vs. asynchronous) was incorporated in the GABA

synapses. Gamma oscillations emerged in the network following external stimulation and subsequent interaction between the pyramidal and interneuron populations. The frequency of network gamma oscillations depended on the strength of coupling between the two neuronal populations. Using this model we studied the dependence of network rhythms on characteristics of synaptic GABA release. Properties of gamma rhythm (location and magnitude of frequency power peak) were modulated by short-term synaptic depression at GABA synapses. Reducing the level of synaptic parvalbumin resulted in de-synchronization of GABA release, thus contributing to de-synchronization of interneuron network activity. Spectral power in gamma range was markedly reduced in parvalbumin-deficient network as compared to the “healthy” network. Removal of parvalbumin from GABA synapses shifted the network rhythm frequency toward beta (20-30 Hz) range. Our study shows that some psychiatric symptoms could be mediated by reduced parvalbumin through impaired synaptic short-term plasticity and increased asynchronous release at GABA synapses of fast-spiking interneurons. Based on these observations, we suggest that plasticity of GABA release could be involved in the etiology of schizophrenia and related neuropsychiatric disorders.

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SCHIZOPHRENIA

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