Varied Organizational Principles Differentially Affect a Model Dentate Gyrus Granule Cell Network's Predisposition to Hyperexcitability

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Following many insults, the mammalian dentate gyrus undergoes dramatic structural rearrangement. Structural changes include the loss of hilar interneurons as well as the sprouting of recurrent connections between granule cells. The functional relevance of these changes has been widely debated, but a vast amount of evidence points to an increase in recurrent excitation that can predispose the neuronal microcircuit to seizure-like activity. Although the phenomenon of mossy fiber (granule cell axon) sprouting has been clearly defined, the principles of organization of the resulting recurrent granule cell network are not understood. By using a biophysically realistic computational model of the dentate gyrus, we have performed simulations that examine how different structural organizational principles (e.g. Hebbian-like rules, three neuron motif frequency differences, scale-free connectivity) affect the predisposition of the network to hyperexcitability. Most structural microcircuitry alterations had little or no effect on the hyperexcitability of the granule cell network. However, implementation of a scale-free topology strongly predisposed the network to hyperexcitability. This result indicates that the presence of a small population of highly connected granule cell "hubs" could promote fast, efficient, and recurrent propagation of activity through the dentate gyrus circuit, thereby creating a pathological entity that is predisposed to seizing.