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Therapeutic rewiring by means of desynchronizing brain stimulation

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In a mathematical model we show that the dynamical multi-stability of a network of bursting subthalamic neurons, caused by synaptic plasticity, has strong impact on the stimulus-response properties when exposed to desynchronizing coordinated reset (CR) stimulation. Such stimuli can reliably shift the network from a stable state with pathological synchrony and connectivity to a stable desynchronized state with down-regulated connectivity.

Finally, the desynchronizing stimulation protocol is tested in two experimental setups: first, we studied long-lasting effects of CR stimulation in rat hippocampal slice rendered epileptic by magnesium withdrawal. We show that the CR stimulation causes a long-lasting desynchronization between hippocampal neuronal populations together with a widespread decrease of the amplitude of the epileptiform activity. In contrast, periodic stimulation control stimulation induces a long-lasting increase of both synchronization and amplitude. Second, we developed appropriate hardware enabling a clinical pilot-study applying coordinated reset stimulation through externalized DBS electrodes to patients suffering from Parkinson's disease. CR stimulation resulted in a long-lasting reduction of the symptoms depicted by clinical motor scores. These theoretical and experimental findings support the idea that desynchronizing stimulation can induce long-lasting effects in neuronal networks featuring dynamical multi-stability.