Coordinated reset (CR) stimulation was developed in order to specifically counteract abnormal neuronal synchrony by desynchronization.

CR stimulation means to deliver phase resetting stimuli at different times to different sub-populations involved in abnormal neuronal synchronization.

Computational studies showed that in neuronal populations with spike timing-dependent plasticity (STDP) CR stimulation has long-lasting, sustained effects.

Coordinated Reset (CR) stimulation was computationally designed to specifically counteract abnormal neuronal synchronization processes by desynchronization. In the presence of spike-timing-dependent plasticity (STDP) this may lead to a decrease of synaptic excitatory weights and ultimately to an anti-kindling, i.e. unlearning of abnormal synaptic connectivity and abnormal neuronal synchrony. The long-lasting desynchronizing impact of CR stimulation has been verified in pre-clinical and clinical proof of concept studies. However, as yet it is unclear how to optimally choose the CR stimulation frequency, i.e. the repetition rate at which the CR stimuli are delivered. This work presents the first computational study on the dependence of the acute and long-term outcome on the CR stimulation frequency in neuronal networks with STDP. For this purpose, CR stimulation was applied with Rapidly Varying Sequences (RVS) as well as with Slowly Varying Sequences (SVS) in a wide range of stimulation frequencies and intensities. Our findings demonstrate that acute desynchronization, achieved during stimulation, does not necessarily lead to long-term desynchronization after cessation of stimulation. By comparing the long-term effects of the two different CR protocols, the RVS CR stimulation turned out to be more robust against variations of the stimulation frequency. However, SVS CR stimulation can obtain stronger anti-kindling effects. We revealed specific parameter ranges that are favorable for long-term desynchronization. For instance, RVS CR stimulation at weak intensities and with stimulation frequencies in the range of the neuronal firing rates turned out to be effective and robust, in particular, if no closed loop adaptation of stimulation parameters is (technically) available. From a clinical standpoint, this may be relevant in the context of both invasive as well as non-invasive CR stimulation [1)].

1)
Manos T, Zeitler M, Tass PA. How stimulation frequency and intensity impact on the long-lasting effects of coordinated reset stimulation. PLoS Comput Biol. 2018 May 10;14(5):e1006113. doi: 10.1371/journal.pcbi.1006113. [Epub ahead of print] PubMed PMID: 29746458.