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Asynchronous, bilateral, and biphasic temporally unstructured electrical stimulation of amygdalae enhances the suppression of pentylenetetrazole-induced seizures in rats

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Highlights

- Desynchronizing electrical stimulation may be used to treat epilepsy.
- Biphasic bilateral asynchronous stimulation has the greatest anticonvulsant effect.
- Morphology, spatial and timing parameters display additive effects.

Abstract

A promising alternative for the treatment of refractory epilepsy is electrical stimulation (ES) of the central nervous system. Based on the premise that epilepsy is a result of neural hypersynchronization, we have previously demonstrated that a novel non-standard form of electrical stimulation with randomized inter-pulse intervals, termed non-periodic stimulation (NPS), applied to the amygdala is robustly anticonvulsant. This investigation also suggested that NPS attains its therapeutic effect by desynchronization of epileptiform activity. Here, we further explored the desynchronization hypothesis by testing how the efficacy of NPS in the suppression of convulsive behaviors depends on morphological, spatial, and temporal parameters of stimulus. For this purpose, we varied the number of pulse phases (monopolar versus bipolar square pulses), side of stimulation (right versus left), number of application hemispheres (unilateral versus bilateral), and interhemispheric temporal synchronicity (synchronous versus asynchronous), while measuring the impact on the anticonvulsant action of NPS. Wistar rats received a controlled infusion of the convulsant agent pentylenetetrazole (PTZ, 10 mg/min), together with one of six variations of NPS applied to the amygdala. A stimulated PTZ-free group of animals was also performed as a positive control. Latency to convulsive behavior was used to measure seizure threshold. Animals receiving NPS displayed significant higher threshold for forelimb clonus and generalized tonic-clonic seizures for all patterns. Thresholds seemed to increase gradually from mono to biphasic, unilateral to bilateral, and synchronous to asynchronous stimuli. Thus, combined biphasic, bilateral, and asynchronous stimulation resulted in the greatest seizure threshold. PTZ free animals did not develop any observable convulsive behavior or other uncommon motor activity.