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Phase response curves in the characterization of epileptiform activity

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Oscillatory coordinated cellular activity is a major characteristic of nervous system function. Recent years have witnessed a surge of interest in the concept that synchronized activity in brain cellular networks plays a crucial role in information processing and behavioural responses. However, adequate frameworks to understand the relation between brain function and behaviour are still underdeveloped. Coupled oscillator theory offers unique avenues to address these questions, as most of the nervous systems can be considered fields of oscillators coupled in different ways. In this study, we focus on the characterization of the dynamics of epileptiform activity, based on some seizures that manifest themselves with very periodic rhythmic activity, termed absence seizures. Taking advantage of this long-lasting periodic activity, our approach consists in obtaining experimentally the phase response curves (PRC), which describe the alteration of the phase due to an input at each point of the cycle, and incorporating these into models of coupled oscillators. To this end, we use a rat model of absence seizures that results from injection with gamma-hydroxybutyric acid (GHB). As a result, very rhythmic synchronized spike-and-wave (SWD) discharges occur in the neocortex and thalamus. Intracerebral recordings are obtained using bipolar electrodes inserted into the cortex and thalamus. Of 42 rats recorded, 17 were used to estimate the PRC. PRCs were obtained by stimulating either the thalamus or the cortex, and evaluating the alteration (advancement or delay) of the oscillation in the cortex or thalamus, respectively. The electrical stimuli used were the minimal that allowed an identification of the stimulating artefact, so that the phase of the stimulation could be calculated, and did not alter profoundly the oscillation. In addition, larger stimulations were tested for their ability to halt the SWD. Only brief (~1 second) stopping (desynchronization) of the SWD was observed in some cases (55%) at large stimulation intensities, phenomenon for which no specific phase of the perturbation was noted. Because these rats have a very low threshold for triggering a SWD, we estimated the instantaneous phase at which a single pulse triggered a seizure, phenomenon which occurred in ~53% of stimulations. Just like in the above case of seizure abortion, no particular instantaneous phase was noted in the pulses that triggered a SWD.

The experimentally obtained PRCs, for the cortex (in response to thalamic stimulation) and thalamus (cortical stimulation) were approximated by a polynomial as well as by a few terms of the Fourier expansion. In our case, these PRCs represent the interaction function between the two oscillators involved in the SWDs: cortex and thalamus. Incorporating these functions into a system of two coupled differential equations representing the time evolution of the respective phases, we are determining the phase preferences of the stationary states and their stability, and these results from the model are compared with the experimental recordings.