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Different Fidelities of Neuronal Responses to Varying Inter-pulse-intervals in High-Frequency Stimulations Applied at Efferent and Afferent Fibers of Hippocampal CA1 Region

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***Abstract*—Electrical pulse stimulation with varying inter-pulse-interval (IPI) provides a new stimulation mode to improve the therapy of deep brain stimulation. However, the fidelity of neuronal reactions to varying IPI remains unclear. In this study, we investigated the differences in the reproduction of neuronal responses to an identical pulse sequence with randomly varying IPI applied at efferent and afferent fibers of rat hippocampal CA1 region in-vivo. Results showed that the stimulation of efferent fiber was able to induce a sequency of antidromically-evoked population spikes (APS) with a high fidelity among different rats, whereas the stimulation of afferent fiber induced various sequences of orthodromically-evoked population spikes (OPS) due to the participation of synaptic transmissions. The results suggest that the immediate neuronal reactions to stimulations of varying IPI are determinative, but the reactions of post-synaptic neurons are variable.**

I. Introduction

Brian stimulations have been used in clinic to treat certain diseases by utilizing high-frequency stimulation (HFS) of electrical pulses. Besides conventional HFS with fixed IPI, HFS with varying IPI has shown a good prospect to improve the therapies [1]. However, the differences in neuronal responses to varying IPI immediately at the stimulation site and at post-synaptic region are not clear. Therefore, in this study, we investigated whether the involvement of synaptic transmissions significantly change the neuronal responses by applying HFS with randomly varying IPI at the efferent fiber and afferent fiber respectively.

II. Method and Materials

The animal experiment was approved by the Institutional Animal Care and Ethics Committee, Zhejiang University. Details of the experiment procedures have been reported previously [2]. An identical 1-min pulse sequence with randomly varying IPI (100 - 200 Hz, mean 133 Hz) was applied at the alveus (efferent) and Schaffer fibers (afferent) of hippocampal CA1 region in 6 rats, termed as A-HFS and O-HFS respectively (Fig. 1A). Amplitudes of APS and OPS following each pulse were calculated to form 6 sequences of APS and OPS, respectively. For the APS or OPS sequences, the similarity between every pair of their amplitude sequences was evaluated by an index of Cosine Similarity (CS) [3].

III. Result and Discussion

Through the whole period of 1-min A-HFS, the APS sequences repeated well in the 6 rats with a mean CS value 0.98 ± 0.01 (Fig. 1B & 1C *left*). However, during 1-min O-HFS, although the initial OPSs induced by the very first pulse were similar (Fig. 1B & 1C *right*), the following OPS sequences were varied among the 6 rats with a mean CS value only 0.56 ± 0.04, significantly smaller than the CS value of A-HFS ($P < 0.01$, *t*-test).

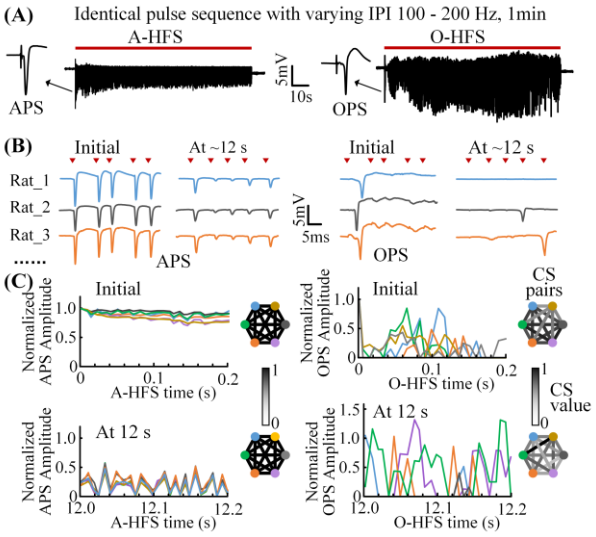

Figure 1. Differences in neuronal responses to HFS with varying IPI applied at efferent fiber (A-HFS) and afferent fiber (O-HFS) of hippocampal CA1 region. (A) Examples of neuronal responses to A-HFS and O-HFS with an identical pulse sequence. (B) Examples of episodes of APS and OPS sequences at initiation and ~12 s of the HFS collected from 3 of the 6 rats. The red inverted triangles indicate the position of stimulation pulses. (C) Episodes of normalized amplitudes of APS and OPS sequences of the total 6 rats, together with a corresponding network on the right, describing the cosine similarity (CS) of pairs of APS or OPS sequences. The darkness of the connection lines in the CS networks indicates the values of CS.

The results suggest that HFS with varying IPI can induce determinative firing at neurons directly under the stimulation. However, through synaptic transmissions, the evoked neuronal activity is diverse and unrepeatable.

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