

High-Frequency Pulse Stimulations at Efferent Fibers Can Decrease Local Inhibitions in Rat Hippocampal CA1 Region

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Abstract—High-frequency stimulation (HFS) of electrical pulses within brain has been developed for treating various brain diseases. However, the underlying mechanisms of the therapy are not completely clear. To investigate the effect of HFS on local inhibitory circuits, we applied antidromic-HFS (A-HFS) at the efferent fibers (alveus) of pyramidal neurons and applied test stimulations of paired-pulse at the afferent fibers (Schaffer collaterals) to induce orthodromic population spikes (OPS). Results showed that the paired-pulse depression (PPD) of OPS disappeared during A-HFS, indicating a suppression of local inhibitions by axonal HFS of efferent fibers.

I. INTRODUCTION

HFS has been utilized by deep brain stimulation (DBS) for treating neurological disorders. Some of previous studies have showed that HFS may increase neuronal firing [1]. We hypothesized that a decrease of local inhibitions could contribute to the firing increase. In this study, we tested the hypothesis by examining the changes of PPD of orthodromic paired-pulse stimulation during A-HFS in the hippocampal CA1 region of anesthetized rats. The results may provide new information for revealing mechanisms of DBS.

II. METHODS

The animal experiment was approved by the Institutional Animal Care and Ethics Committee, Zhejiang University. Seven Sprague-Dawley rats were used. The methods of rat experiment and data analyses were similar to previous reports [1]. Paired-pulses with a 50 ms interval were applied at Schaffer collaterals before, during (one per 10 s) and after the 1-min 100 Hz A-HFS (Fig. 1A & 1B). The amplitude ratio of OPS_2/OPS_1 was utilized to evaluate the PPD.

III. RESULTS AND DISCUSSION

During baseline, the OPS_2 of paired-pulse was very small resulting a small ratio of OPS_2/OPS_1 (i.e., PPD) because the OPS_2 was suppressed by intact local inhibitions (Fig. 1B b1 & 1C). However, during a 1-min A-HFS, when the antidromic population spikes (APS) induced by the pulses of A-HFS decreased markedly, the OPS_2 grew even larger than OPS_1 . The mean ratio of OPS_2/OPS_1 was significantly greater than baseline during the 1-min A-HFS and then returned to

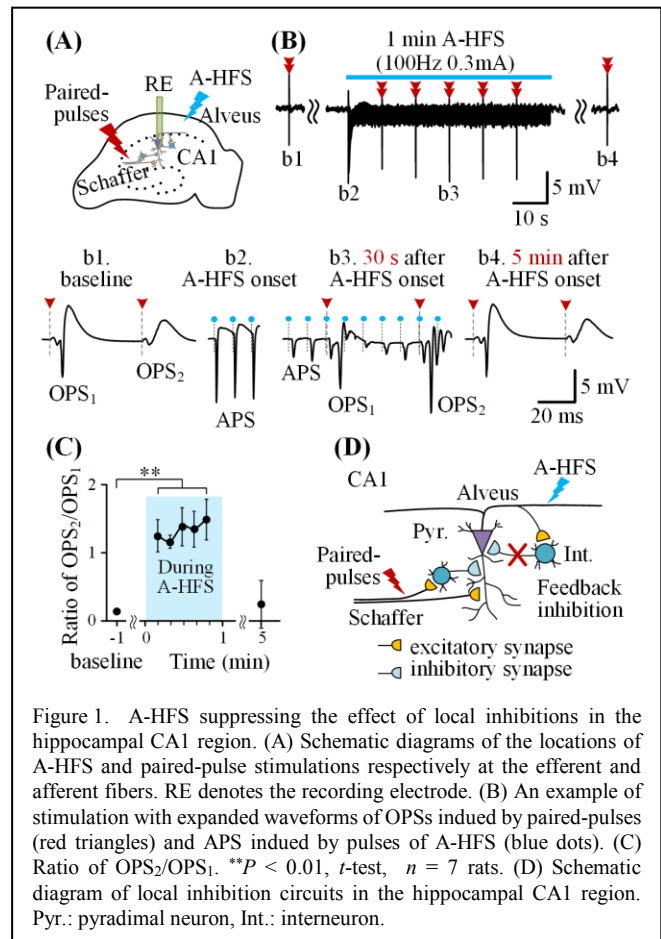


Figure 1. A-HFS suppressing the effect of local inhibitions in the hippocampal CA1 region. (A) Schematic diagrams of the locations of A-HFS and paired-pulse stimulations respectively at the efferent and afferent fibers. RE denotes the recording electrode. (B) An example of stimulation with expanded waveforms of OPSs induced by paired-pulses (red triangles) and APS induced by pulses of A-HFS (blue dots). (C) Ratio of OPS_2/OPS_1 . ** $P < 0.01$, t -test, $n = 7$ rats. (D) Schematic diagram of local inhibition circuits in the hippocampal CA1 region. Pyr.: pyramidal neuron, Int.: interneuron.

baseline level in 4 min after the end of A-HFS (Fig. 1B, b2 - b4 & 1C). Moreover, the OPS of paired-pulses appeared as multiple spikes during A-HFS.

These results indicated that sustained A-HFS suppressed the effect of local inhibitions. It has been shown that intense activations can impair the inhibitions of GABAergic synapses [2]. Presumably, an intense firing of interneurons under the activation of A-HFS may cause a decrease of feedback inhibitions (Fig. 1D, the red cross) thereby enhancing the excitability of the somata of pyramidal neurons.

REFERENCES

- [1] Z. Feng, Z. Wang, Z. Guo, et al. "High frequency stimulation of afferent fibers generates asynchronous firing in the downstream neurons in hippocampus through partial block of axonal conduction," *Brain Research*, vol. 1661, pp. 67-78, 2017.
- [2] K. J. Staley, B. L. Soldo and W. R. Proctor, "Ionic mechanisms of neuronal excitation by inhibitory GABAA receptors," *Science*, vol. 269, pp. 977-81, 1995.

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