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Changes of Neuronal Reactions Around Soma During High-Frequency Stimulation at Axons in Hippocampus CA1 Region

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***Abstract*—High-frequency stimulation (HFS) of electrical pulses has been used in deep brain stimulation (DBS) to treat certain brain disorders successfully. However, the effects of HFS on neurons are not completely clear yet. In this study, we utilized recordings of electrode array and the method of current source density (CSD) analysis to investigate the changes of neuronal reactions around somata when their axons were under sustained antidromic HFS (A-HFS). The result showed that, in addition to the axonal blockage reported previously, the propagation speed of current sink around somata significantly decreased during the A-HFS. The finding indicated a change at the neuronal soma caused by sustained axonal HFS.**

I. INTERODUCTION

The underlying mechanisms of sustained pulse HFS on neurons have been investigated extensively in recent years. Previous studies have shown a mechanism of depolarization blockage on axons by HFS with multiple dynamics [1]. We hypothesized that sustained axonal HFS could simultaneously cause a change around the soma of neurons, and tested the hypothesis by utilizing CSD analysis to measure the changes of generation and propagation of action potentials around somata during axonal HFS.

II. METHODS

The experimental protocol was approved by the Institutional Animal Care and Ethics Committee, Zhejiang University. Adult male Sprague-Dawley rats were used for *in-vivo* recordings. Procedures of animal surgery, stimulation, data collection and data analysis were similar to previous report [1]. During a 2-min A-HFS of 100 Hz pulse at the alveus, the axons of pyramidal neurons of hippocampal CA1 region, a gap of 20 ms was inserted every 8 s in the late 80 s period of A-HFS (Fig. 1A). The evoked potentials around the pyramidal layer of CA1 region were recorded by a 16-channel electrode with a 25 μm spacing perpendicularly, including the antidromically-evoked population spikes (APS) at the pyramidal cell layer. Then, the CSD signals of the evoked potentials were calculated [2]. The latency of CSD sink at the soma and the propagation speed of CSD sink around soma were calculated.

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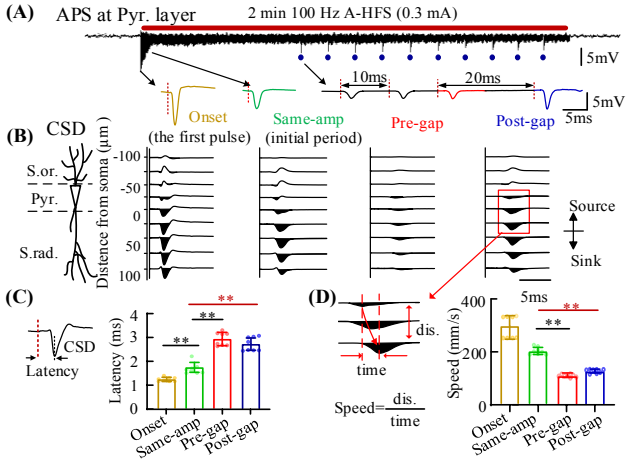

Figure 1. Changes of latency and propagation speed of CSD sinks of evoked potentials around somata during A-HFS in the hippocampal CA1 region. (A) An example of evoked APS recorded at the pyramidal cell layer of hippocampal CA1 region. (B) Examples of CSD at the times of A-HFS onset, initial period, preceding a gap (Pre-gap) and following a gap (Post-gap). The APS at the initial period was chosen to have an amplitude similar to the Post-gap APS. (C) and (D) Comparisons of the latencies and propagation speeds of CSD sinks among the four different times. $^{**}P < 0.01$, one-way ANOVA with Post hoc Bonferroni, $n = 8$ rats.

III. RESULTS AND DISCUSSION

At the onset of A-HFS, the CSD sink of the first evoked potentials appeared firstly at axon hillock, then propagated to soma and dendrites. After 40 s of stimulation, the CSD sinks decreased with the substantial decrease of APS amplitudes (Fig. 1A & 1B). To reveal the changes of soma except the axonal blockage, we compared the CSD sink following a gap of 20 ms when APS partially recovered and the sink of an APS with the same amplitude appeared within initial 1-s period of A-HFS. The mean latency of the sink of Post-gap potentials was significantly longer than that of initial period (Fig. 1C). In addition, the propagation speed of CSD sink of Post-gap was significantly slower than that of initial period (Fig. 1D).

The increase of the latency and the decrease of propagation speed indicated that sustained axonal HFS may also slow down the actions around neuronal somata.

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