2021 43rd Annual International Conference of the
IEEE Engineering in Medicine & Biology Society (EMBC)
Oct 31 - Nov 4, 2021. Virtual Conference

Accumulation of non-synaptic and synaptic excitations induced by microstimulation pulses in the mouse visual cortex layer II/III

Santa Fukuda, Tomohiro Nomoto, Kou Yoshida, Yuki Hayashida, *Member*, EMBS, and Tetsuya Yagi

***Abstract*—Cortical voltage responses to repetitive micro-stimulation pulses in the primary visual cortex layer II/III were examined in the mouse cerebral slices. The stimulus-induced excitations were composed of the accumulated and the responsive components, which were attributable to those with the non-synaptic and synaptic mechanisms.**

I. INTRODUCTION

The intracortical microstimulation is considered as a means of controlling neural circuits for alleviating cortical dysfunctions, such as for visual prostheses [1]. Our previous study showed that the single microstimulation pulse delivered to the primary visual cortex initiates action potential firing of neuronal population in the vicinity to the stimulating electrode tip in a few milliseconds, which then activates the downstream excitatory and inhibitory circuits to confine the excitation in a local spatial region [2]. This single-pulse response dynamics provides a possible underlying mechanism for the localized phosphenes induced by the microstimulation in humans [1]. However, cortical responses to trains of the microstimulation pulses delivered at high frequency, which have been used in the human and non-human primate studies [1][3], may not be simple linear convolutions of the single-pulse response. Therefore, in the present study, we analyzed the response dynamics during high-frequency train stimulations in the mouse cerebral slices by means of the voltage-sensitive dye (VSD) imaging at the millisecond scale.

II. METHODS AND RESULTS

Animal experiments were performed under approval by the Animal Experiment Committee of Osaka University and in accordance with the Guidelines for Proper Conduct of Animal Experiments by the Science Council of Japan. The experimental methods were similar to those of the VSD imaging in the previous study [2], except that 1) the microstimulation pulses were delivered at either 50 or 200 Hz to the layer II/III, 2) the imaging area was 154 × 820 μm on the slice and 12 × 64 binned-pixels of the CCD sensor, in which the acquisition rate was 1000 fps. The data sets obtained for four slices were analyzed and averaged to be shown in the figure.

Fig. 1*A-B* shows time courses of the VSD signal (i.e., the fractional intensity changes of the light transmitted through the VSD-stained slice [2], denoted as $\Delta T(t_n)/T_0$ in the figure) in the vicinity to the stimulating electrode tip through which the microstimulation pulses (either 20 or 40 μA/phase in amplitude) were delivered at either 50 (*A*) or 200 Hz (*B*). The traces obtained in the control condition (green), in the presence of 20-μM D-AP5 (blue), and in the presence of both 20-μM D-AP5 and 10-μM DNQX (or CNQX) (red) are superimposed in each of the panels. As shown here, the increase in the VSD signal, which corresponded to membrane depolarization, was induced by each of the stimulation pulses, and was accumulated during the train stimulation with either of the frequencies. The pharmacological tests showed that the accumulation of the excitation involved synaptic circuitries with NMDA and non-NMDA glutamate receptors. Also, the excitation was accumulated under the blockade of glutamate receptors. The accumulating responses appeared to reach plateau levels after approximately 60 msec. Fig. 1*C-D* shows spatial profiles of the VSD signal along the axis parallel to the layer plane. Each of these profiles was calculated as the average of those for the time points immediately before the stimulation at 60, 80, and 100 msec (solid lines) (referred to as accumulated component), or for the time points when the responses to the three stimulation pulses reached the peak (dotted lines) (referred to as responsive component). As shown here, the spatial profiles appeared to consist of the accumulated and the responsive components, both of which were attributable to non-synaptic excitations and the synaptic excitations. Possible roles of electrical and inhibitory synapses, and/or glial cells in shaping the excitation accumulation remained to be examined.

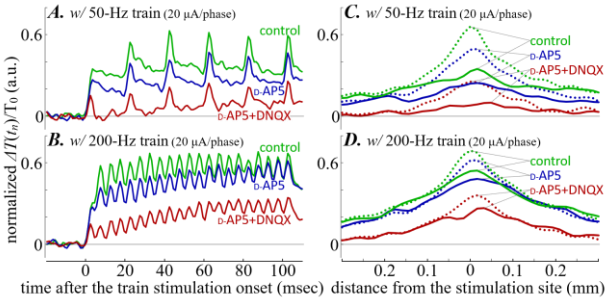

Figure 1. Cortical voltage responses to the train stimulations.

REFERENCES

[1] E. M. Schmidt et al., "Feasibility of a visual prosthesis for the blind based on intracortical microstimulation of the visual cortex," Brain vol. 119 (2), pp. 507-522, 1996.

[2] Y. Tanaka et al., "Focal activation of neuronal circuits induced by microstimulation in the visual cortex," J. Neural. Eng., vol. 16 (3), 036007 (17 pp.), 2019.

[3] X. Chen et al., "Shape perception via a high-channel-count neuroprosthesis in monkey visual cortex," Science, vol. 370 (6521), pp.1191-1196, 2020.

*Research partly supported by JSPS KAKENHI Grant Number JP20H00606, JP18K12059.

S. F. is with Grad. Eng., Mie Univ., Tsu, Mie 514-8507, Japan. T. N. and K. Y. are with Grad. Eng. Osaka Univ., Suita, Osaka 565-0871, Japan. T. Y. is with Grad. Eng., Osaka Univ. and with Sch. Eng., Fukui Univ. Tech., Fukui, Fukui 910-8505, Japan. Y. H. is with Grad. Eng., Osaka Univ. and with Grad. Eng., Mie Univ. (hayashida@ai.info.mie-u.ac.jp).