RAPID DRUG MICROADMINISTRATION TOWARD NEURON USING ELECTROCHEMICAL MICROPUMP FOR BRAIN THERAPY

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1. INTRODUCTION

A brain is sophisticated and complex system composed of distinct functional regions. The minimum neuron has independent function. Most of disorders of brain (e.g. Parkinson's disease, epilepsy) is due to damage of specific region.

For effective chemical therapy of brain disorders, micro-administration of drug toward selected area and time must be developed. Although micropumps for delivering chemical stimulant are already on practical use, these experiment tools need complicated mechanics and wiring. We then developed a simple micropump which jets out inner solution rapidly by bubbling resulted from electrolysis of water[1]. We improved the electrochemical micropump and tried microadministration using the pump toward identified cell with monitoring response of the membrane potential.

2. MATERIALS AND METHODS

The simple structure of the pump is good for downsizing and integration. The micropump consists of a glass capillary (O.D. 1.5mm) with a tip of 1 μm in diameter in which platinum wires were inserted as electrodes. It was filled with neurotransmitter solution and sealed by hot glue as shown in Fig. 1.

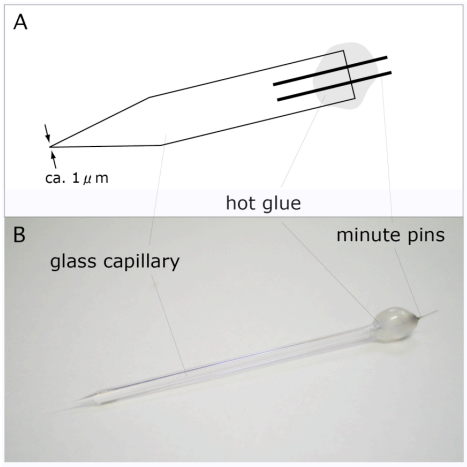

Fig. 1 Structure of micropump

We used Aplysia's L7 (motor neuron in Abdominal ganglion: Fig. 2) as a model cell which is sensitive to glutamate released from sensory neuron. The micropump, which was filled with 10mM glutamate, was placed close (< 10 μm) to L7 dendrite. A potential difference of 3.0V was applied to the electrodes when administering glutamate. Neuronal potential change of L7 was recorded by conventional electrophysiological measurement.

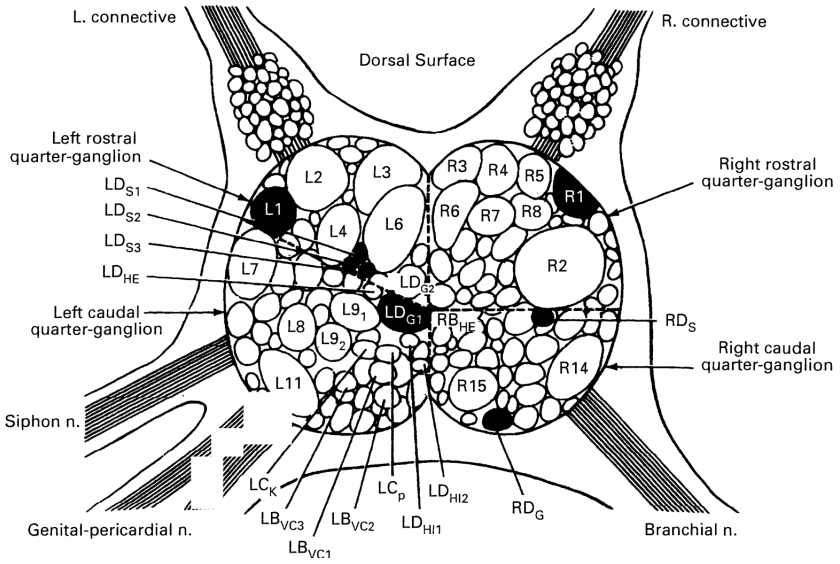

Fig. 2: An abdominal ganglion [2]

Each glutamate administration generated an Excitatory Post Synaptic Potential (EPSP) in real time. The EPSP decreased gradually with successive administration. This lowering of EPSP is thought to be due to glutamate receptor's desensitization. Then this method may be useful for basic study of learning and memory as well as an artificial sensory neuron. Additionally it will enable sophisticated drug administration toward neuron or identified region in brain. However, this method needs a method of strict control of injection which avoids accumulation of the excess neurotransmitters or drugs around the target neuron after injection. We do not think such a method is extremely difficult because electrochemical reaction is generally controllable by current or potential. The authors will design the structure and operation of the pump by chemical engineering methodology.

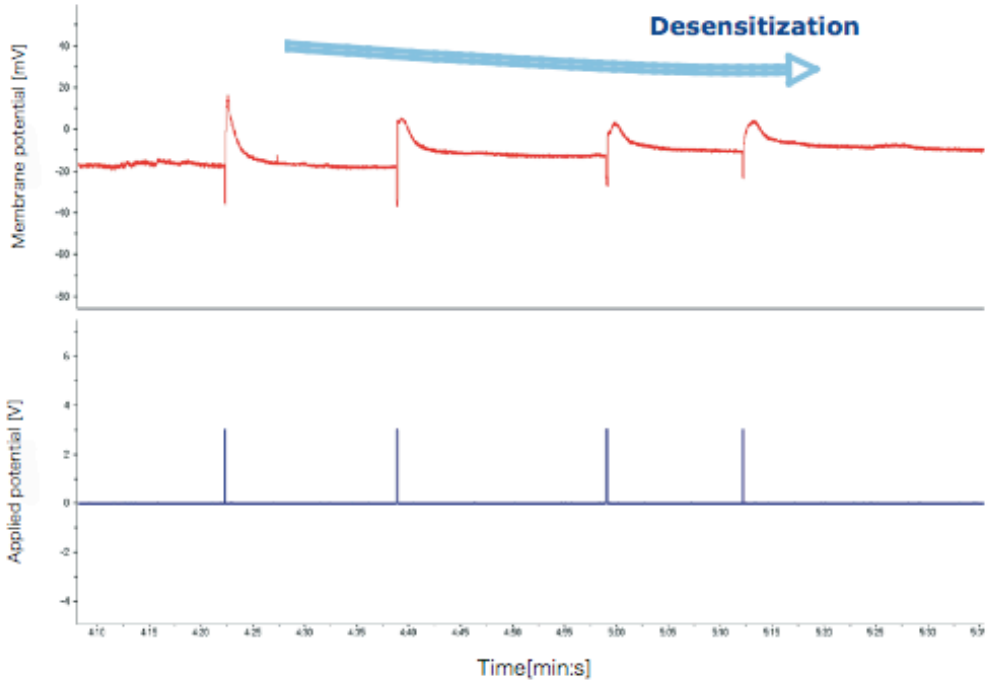

Fig. 3: Time course of membrane potential (upper) and applied potential toward electrode in the micropump filled with sodium glutamate solution.

REFERENCES

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