

## HIPPOCAMPAL MICROSTIMULATION INHIBITS MICTURITION REFLEX IN URETHANE-ANESTHETIZED RATS

### Hypothesis / aims of study

Hippocampus is known to be involved in emotion and memory functions. Although recent brain imaging studies have indicated the activation of hippocampus during micturition control, there is no report that directly examines the role of hippocampus in micturition reflex. The purpose of this study is to investigate how direct stimulation of hippocampus affects the micturition reflex.

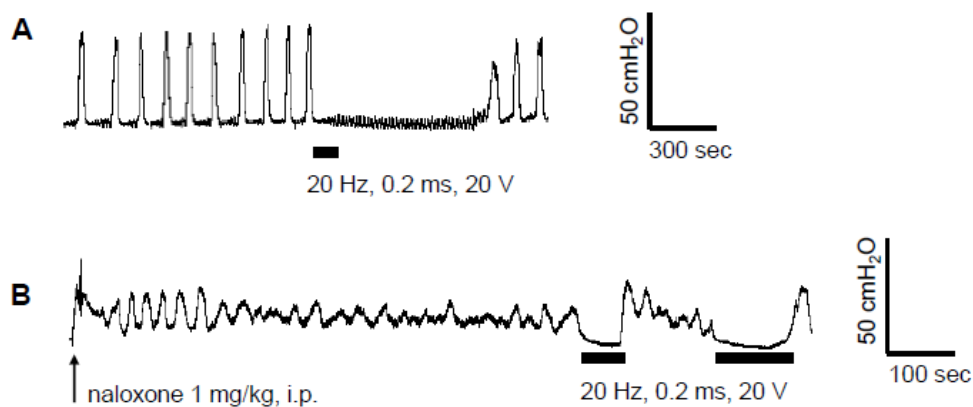
### Study design, materials and methods

A total of 8 female Sprague-Dawley rats weighing 300g under urethane anesthesia (1.2 g/kg) were used in this study. The bladder was cannulated through urethra using a PE-50 catheter, and isovolumetric bladder contractions were recorded. After the catheter insertion, rat was fixed on a stereotaxic frame and then the brain was exposed by removing a small piece of skull. A concentric tungsten electrode was inserted stereotaxically into the hippocampus following the coordinates of the rat brain map by Paxinos and Watson. An electrical stimulation (0.2 ms pulse width and 20 V) with frequencies from 1 to 200 Hz was applied to the hippocampus to evaluate its effect on isovolumetric bladder contraction. After the stimulation, the brain was resected and preserved in the formalin for histology.

### Results

An electrical stimulation of 20 Hz frequency maximally inhibited the isovolumetric bladder contractions with the microelectrodes in the dorsal areas of hippocampus. The inhibition lasted for a much longer time than the stimulation duration (Figure A). Intraperitoneal administration of naloxone (1 mg/kg) shortened the duration of inhibition, but it did not completely eliminate the inhibition. The stimulation never induced any excitatory response (Figure B).

### Effect of the hippocampal electrical stimulation on isovolumetric contraction in urethane anesthetized rats



Effect of the hippocampal electrical stimulation on isovolumetric contraction in urethane anesthetized rats. A. Inhibitory effect of 20-Hz-hippocampal electrical stimulation on isovolumetric bladder contraction. B. Effect of naloxone on hippocampal inhibition of isovolumetric contraction. The duration of hippocampal stimulation is indicated by the black bar under the bladder pressure trace.

### Interpretation of results

Using a functional magnetic resonance imaging (MRI), Tai et al. reported the activation of hippocampus during bladder contraction in anesthetized rats, while this area is inactive during bladder filling. In a rats study, the hippocampus is reported to be labelled with a tracer after the injection of pseudorabies virus into the bladder [1]. The hippocampal activation during micturition is also reported in human imaging studies [2, 3]. Taking these findings into consideration, it can be assumed that the hippocampus has a role in the mechanism of controlling micturition reflex. Because no direct synaptic connection between hippocampus and micturition center has been known until today, it may be composed of indirect pathways. In the present study, naloxone shortened the inhibition after the hippocampal stimulation, but it did not completely eliminate the inhibition. Thus, the enkephalinergic pathway in the brain is suggested to be partially involved in this inhibition.

### Concluding message

These results suggest that the electrical activation of neurons in the hippocampus inhibits the micturition reflex. Understanding the brain function in micturition control is important for the treatments of bladder dysfunctions caused by brain damages or disorders.

### References

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### Disclosures

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