Implantable micro-imaging device for visualizing neural activity in regions related to feeding behavior

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I. Introduction

Feeding behavior results from a complex interplay between multiple control systems spanning neural circuits that are known to be involved in the processing of reward and pleasure. Currently, visualizing neural activity from calcium dynamics in the deep brain area remains difficult to implement without influencing the behavior of an awake mouse. To this end, we have developed an implantable micro-imaging device that can visualize neural activity from calcium dynamics in the deep brain [1]. In this abstract, we report a measurement of feeding behavior by applying the device and show successful results from the experiments.

II. Freely moving experimental results using the implantable micro imaging device

The micro-imaging device that we have developed consists of a CMOS-based image sensor chip embedded on a flexible substrate and a μ-LED that serves as an excitation light source [1]. The fabricated devices have been implanted into the deep brain of transgenic mice (**Fig 1**), GCaMP6 mice in particular, and demonstrated successful detection of neuronal activity in the lateral and the arcuate nucleus of the hypothalamus, sections of the striatum, and the amygdala [2]. These deep regions are strongly related with feeding behavior. The increase in neuronal activity is marked by a rise in fluorescence intensity detected from cell bodies expressing GCaMP6, a genetically-engineered calcium-binding protein whose fluorescence is modulated by changes in intracellular [Ca^{2+}].

Early *in vivo* imaging results indicate distinct patterns of activity during various behavioral states, as shown in **Fig 2**. In this figure, representative $\Delta F/F_0$, the ratio of fluorescence intensity is mapped in the timeline of animal behavior. The results clearly indicate neuronal activity in the lateral hypothalamus (LH) obtained *in vivo*. We have developed a monitoring system to compare the animal behavior and neuronal activities in real time. All of animal experiments were performed based on a regulation of animal experiment in NAIST.

Compared to extant imaging systems, advantages in our design include: (1) reduced invasiveness due to its streamlined needle-like design, (2) fluorescence measurements under the freely moving condition with minimum stress because of the light weight (~0.02 g), and (3) simultaneous implantability at multiple points for the study of neuronal networks due to the miniaturization.

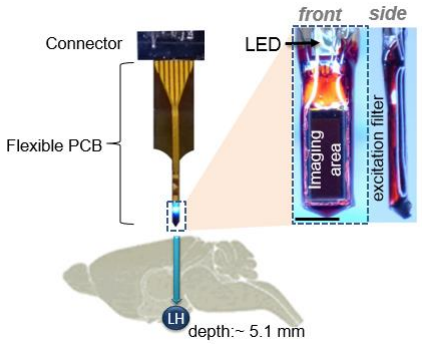

Fig 1. Schematic of implantation site of the micro-imaging device in the mouse deep brain. This sample site in the figure is the lateral hypothalamus (LH), situated approximately 5.1 mm ventral from the bregma. Zoomed-in region indicates the respective positions of the μ-LED and the imaging area. The scale bar is 500 μm.

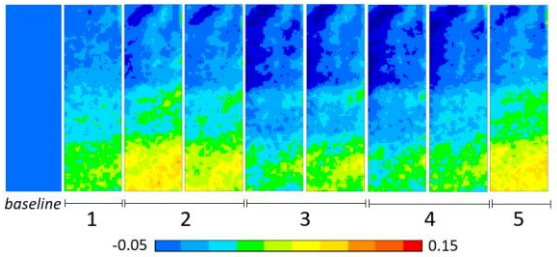

Fig 2. Representative $\Delta F/F_0$ fluorescence intensity maps indicating neuronal activity in the lateral hypothalamus (LH) obtained *in vivo*. Pseudo color reference values are given on the bottom scale. Observed behavioral states labeled 1–5, 1:awake quiescent, 2: walking, 3: feeding, 4: grooming, 5: walking. Intervals between frames vary only to show distinct activity derived from pertinent behaviors.

III. Conclusions

We implanted our developed device into the lateral hypothalamus (LH), a region related to feeding behavior, as a preliminary result and succeeded in measuring fluorescence of neuronal activity, and succeeded to grasp the detailed meaning of neuronal activity by newly incorporating the method of displaying the imaging of animal's behavior and fluorescence image side by side.

Acknowledgements

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References

[1] J. Ohta *et al.*, Proc. IEEE, 105(1), 158, 2017.
[2] M.C. Guinto *et al.*, Annual Meeting of Society for Neuroscience 2018