Tokyo, 7 October - **Juntendo University researchers identify layer specific activity for the first time during cued recall in monkeys performing object association. The findings are published in the journal Neuron, 7 October 2016.**

The area of the brain responsible for higher neural functions, such as memory and attention, is the cerebral cortex. However the mechanism behind information processing for these functions has not been understood. A recent report from researchers at Juntendo University, the University of Tokyo and CREST has now identified some characteristics of the mechanisms behind these functions in macaque monkeys.

The cerebral cortex is divided into six horizontal layers. As Yasushi Miyashita and colleagues point out in the report, “A key question is whether different types of memory-related neurons are situated in distinct layers or distributed throughout cortical layers.” However distinguishing activity in different layers has so far been inhibited by difficulties in locating neuron activity at adequate resolution.

Previous studies have relied on small regions of tissue damage from electronic pulses – electrolytic lesions – to identify where electrodes had penetrated to compare neural activity with structural information observed in microscopic images of slices of the brain post mortem. However, the lesions fade too fast for the longer studies needed to investigate behaviour like cued-recall in memory tasks.

Instead the researchers compared MRI images of electrodes recording neural activity with structural images of brain slices. The elgiloy electrodes left metal deposits that were visible on both MRI and microscopic images allowing ready comparison.

Miyashita and colleagues noted neural patterns for cue holding and paired-recall during object association tasks and found that the cue holding index was greater in the top most layers of the

cerebral cortex (layers 1-4) and paired recall was greater in the bottom most (layers 5 and 6). Further distinctions in activity timing were noted between the neurons in layers 5 and 6 and within two subgroups of neurons in layer 6. The results suggest neural coding processes that differ from those identified in primary sensory cortices.

Background

Brain structure

The brain largely consists of white matter surrounded by the cerebral cortex, a sheet of neural tissue that is folded to a greater and greater extent in larger mammals. The cerebral cortex is divided into four lobes, within which different cortical areas are responsible for different functions.

While previous investigations have shed some light on the neural coding of the brain's primary regions for the five senses, the activity in the six different layers for higher-level cognition such as memory and attention has been little understood. What was known is that information that arrives in the brain is processed by local circuits or "canonical microcircuits" that traverse these laminar layers.

Combining MRI and histology

The laminar structure of the cerebral cortex is visible when slices of brain taken from the animal after it has been killed are viewed under a microscope, a process described as histology. However using lesions from electric pulses as indicators to align the position of recorded neural activity with histological images causes problems for studies of higher neural functions. The lesions fade faster than the experiment and recording several channels leads to non-negligible tissue damage.

Instead Miyashita and colleagues found a metal deposit mark left by the electrode was visible on both MRI and *post mortem* histological images. This way the neural activity observed could be aligned with the laminar structure to identify the laminar location of the neurons fired.

Cued-Recall

In memory there are three main types of recall: free recall such as the repeating of a list of memorised items in any order; serial recall, which includes the ability to repeat the order of the items as well; and cued recall whereby an item is recalled when cued by something that has become associated with it through training.

The macaque monkeys were trained to associate pairs of visual objects so that being presented with one from the pair would cue recall of the other. The neural activity during such cued recall tasks could then be monitored.

Reference

Kenji W Koyano[1], Masaki Takeda[1,2]*, Teppei Matsui[1], Toshiyuki Hirabayashi[1], Yohei

Ohashi[1] and Yasushi Miyashita[1,2,3]*†, Laminar module cascade from layer 5 to 6 implementing cue-to-target conversion for object memory retrieval in the primate temporal cortex, 2016 *Neuron (published online 7 October 2016).*

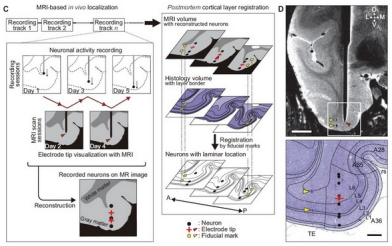
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1. Department of Physiology, The University of Tokyo School of Medicine, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan.
2. Juntendo University School of Medicine, 2-1-1 Hongo, Bunkyo-ku, Tokyo 113-8421, Japan.
3. Core Research for Evolutional Science and Technology (CREST), Japan Science and Technology Agency (JST), Kawaguchi, Saitama 332-0012, Japan.

*corresponding authors e-mail mtakeda-ns@umin.ac.jp or yasushi_miyashita@m.u-tokyo.ac.jp

†Lead Contact



Caption

Localization procedure of recorded neurons at the resolution of six cortical layers. In ‘MRI-based *in vivo* localization’ of recorded neurons in each recording track (left column), the microelectrode-tip position was localized in MRI scan sessions and the locations of recorded neurons were reconstructed in the MRI volume by referring to the locations of the microelectrode-tip. After completion of all the recordings, the neurons in the MRI volume were registered onto the *postmortem* histological volume by aligning both of these volumes with the aid of metal deposit marks that served as common references visible in both the MRI

volume and the histological volume. Black dot, recorded neuron; red cross and arrowhead, electrode tip; yellow dot and arrowhead, elgiloy-deposit fiducial mark.

About Juntendo University

Mission Statement

The mission of Juntendo University is to strive for advances in society through education, research, and healthcare, guided by the motto “Jin – I exist as you exist” and the principle of “Fudan Zenshin - Continuously Moving Forward”. The spirit of “Jin”, which is the ideal of all those who gather at Juntendo University, entails being kind and considerate of others. The principle of “Fudan Zenshin” conveys the belief of the founders that education and research activities will only flourish in an environment of free competition. Our academic environment enables us to educate outstanding students to become healthcare professionals patients can believe in, scientists capable of innovative discoveries and inventions, and global citizens ready to serve society.

About Juntendo

Juntendo was originally founded in 1838 as a Dutch School of Medicine at a time when Western medical education was not yet embedded as a normal part of Japanese society. With the creation of Juntendo, the founders hoped to create a place where people could come together with the shared goal of helping society through the powers of medical education and practices. Their aspirations led to the establishment of Juntendo Hospital, the first private hospital in Japan. Through the years the institution’s experience and perspective as an institution of higher education and a place of clinical practice has enabled Juntendo University to play an integral role in the shaping of Japanese medical education and practices. Along the way the focus of the institution has also expanded, now consisting of four undergraduate programs and three graduate programs, the university specializes in the fields of health and sports science and nursing health care and sciences, as well as medicine. Today, Juntendo University continues to pursue innovative approaches to international level education and research with the goal of applying the results to society.