【Grant-in-Aid for Transformative Research Areas（B）】

Section III

Title of Project： Morphological features and gene expression patterns underlying hub neurons

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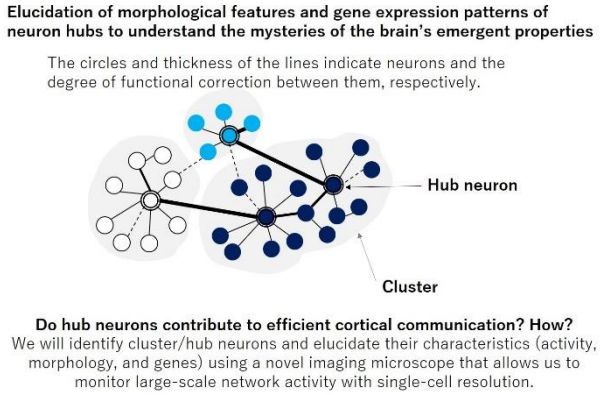
Number of Research Area：20B305　Researcher Number：30578901

【Purpose of the Research Project】

Neurons with high-ranking functions in each brain region are considered hub neurons. These neurons influence many other neurons and are thought to contribute to the efficiency of interactions between the regions. To unravel the mystery of the brain's emergent properties, we believe that it is essential to elucidate the cortico-cortical interaction mechanisms based on hub neurons. Therefore, it is necessary to observe brain-wide activity at the single-cell level; however, due to technical limitations, it has been difficult to develop such a method. In this research project, we will use a new microscope that allows us to monitor large network activity with single-cell resolution and try and answer critical questions, such as (1) whether hub neurons are associated with efficient cortical communications, (2) what factors predestine them to be hub neurons? and (3) what morphological features and gene expression features make them hubs? We aim to understand the morphological features and gene expression patterns that determine a neuron hub.

【Content of the Research Project】

Using the unique microscope developed by us, we will perform fast and wide field-of-view (FOV) two-photon Ca^{2+} imaging to elucidate the contribution of hub neurons to efficient cortical communication. We will proceed with a multidisciplinary approach involving collaboration with neurophysiology, statistical physics, and bioinformatics.



Goals

(1) Development of cluster/hub identification algorithms for large-scale data: [A] Validation by manipulation of hub neurons [B] Estimation of neural network/cluster structure and hub cells.

(2) Development of a multidisciplinary approach to identify factors (morphology, genes) that define hub cells: [A] Development of a platform to extract soft and hard factors from data [B] Identification and biological interpretation of factors that determine hubness.

(3) Estimation of hub neurons by transcriptome first approach for disease model application: [A] Construction of hub/non-hub neuron classifiers [B] Identify diseases that increase/decrease hub neurons.

【Expected Research Achievements and Scientific Significance】

The factors and pathogenic mechanisms responsible for psychiatric disorders have not yet been identified. If the critical factors that determine a neurons hub in cortico-cortical communications are clarified, it may be possible to explain the pathogenesis of psychiatric disorders by focusing on the characteristics of hub cells, allowing us to propose new therapeutic interventions and to develop methods for the early diagnosis of psychiatric disorders. We also expect to discover a group of genes related to psychiatric disorders that has not been identified till date. This research also involves a biochemical approach to characterize the molecular function of each gene's products. The biochemical examination of the newly discovered gene groups' molecular characteristics will enable identification of previously unknown marker genes. Furthermore, since this research also includes physiological approaches to explore the role of hub cells in brain functions such as perception, cognitive functions, and memory, collaboration with researchers from different fields is expected.

【Key Words】

Wide FOV two-photon microscope: The FOV of the conventional two-photon microscope, which detects neural activity in vivo as fluorescence changes, is approximately 0.5 x 0.5 mm^2. Our novel wide FOV two-photon microscope expands this FOV to 3 x 3 mm^2, 36 times larger than that of the conventional microscope. Using this microscope, we can record the activity of about 16,000 neurons from multiple brain regions simultaneously. This number is the largest in the world at present. This large-scale recording will allow us to identify many rare hub cells with high accuracy and enable network analysis at the cellular level.

【Term of Project】

FY2020-2022

【Budget Allocation】

122,400 Thousand Yen

【Homepage Address and Other Contact Information】

https://cluster-hub-dynamism.com/
https://twitter.com/ClusterHub_D