Mouse Cell Type-Specific Brain Mapping in Health and Disease

https://neurodegenerationresearch.eu/survey/mouse-cell-type-specific-brain-mapping-in-health-and-disease/

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Title of project or programme

Mouse Cell Type-Specific Brain Mapping in Health and Disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 3,131,744.04

Start date of award

15/05/2014

Total duration of award in years

3

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Bioengineering... Biomedical Information Resources... Biomedical Information Resources and Informatics Research... Brain Disorders... Dementia... Neurodegenerative... Neurosciences

Research Abstract

DESCRIPTION (provided by applicant): Anatomical circuitry is the foundation by which information travels within the brain. Therefore, comprehensive wiring diagrams are fundamental for understanding how circuits control complex behavioral and cognitive processes. However, only sparse connectivity datasets exist for mammalian model species, and most are collated from tract tracing literature. This is problematic due to the large variety of methods, targeted areas, nomenclature, and assessment of connection strengths by different labs. Instead, at the Allen Institute, we created an entirely new, standardized, publicly and freely available, dataset (Mouse Connectivity Atlas; ://connectivity.brain-map.org) based on modern anterograde axon tracing and high-throughput 2-photon imaging methods to visualize inter-areal and genetically defined cell type-specific projections across the entire young adult mouse brain from ~300 regions. The Mouse Connectivity Atlas data reveals general organizational principles in healthy brains, but many details are still missing. For example, subclasses of neurons within a region projecting to either single or multiple targets are not always defined, nor are the layers of origin of cortical input neurons to specific targets defined. Higher resolution descriptions of structural connection patterns at the cell type, rather than areal, level will enable more accurate modeling and hypotheses on cortical information processing and cognition in health and disease. In neurodegenerative diseases that rob patients of cognitive abilities, such as Alzheimer's disease (AD), pathology spreads in selectively vulnerable regions in specific patterns that resemble, but do not exactly duplicate, network architecture. Taking into account specific cortical projection pathways could thus provide a better structural framework for understanding, predicting, and treating disease. We propose to enhance the Mouse Connectivity Atlas through focused anatomical tracing of whole-brain axon pathways from neurons defined by their projection targets within and outside of disease- relevant large-scale cortical networks. This will be accomplished through the development of a combined viral- based retrograde and anterograde intersectional fluorescent labeling strategy, and our established, successful high-throughput imaging and informatics platform. We will densely survey and map cell type projections defined by target regions in the mouse default mode-like and hippocampal networks, which participate in essential normal cognitive tasks and are vulnerable to AD. New data will be integrated into Allen Institute online resources, providing external users access to raw 2-D images, annotated 3-D projection models, and other analysis tools. We will specifically test the prediction that anatomical classes of projection neurons within an area belonging to the functionally-defined default mode network preferentially connect to other areas within the network. We also propose to use this foundational dataset as a guide for generating and analyzing a brain- wide cell type structural connectivity matrix for an AD mouse model, which could facilitate research in the AD community on disease-related network dysfunction and propagation of pathology.

Lay Summary

PUBLIC HEALTH RELEVANCE: Modern brain mapping projects share a goal of creating circuit diagrams with more detail than previously possible, expecting that any additional information will help illuminate functional implications of healthy brain organization and network breakdown in disease. We will develop and apply new, high-throughput methods for adding critical details of anatomical connections formed by specific neuron types in large-scale networks involved in cognition, and map brain-wide structural connectivity patterns in a widely used mouse model of Alzheimer's disease.

Further information available at:

Types:

Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

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N/A