

Highly evolved brain circuits in primates: molecular vulnerabilities for disease

<https://neurodegenerationresearch.eu/survey/highly-evolved-brain-circuits-in-primates-molecular-vulnerabilities-for-disease/>

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Contact information of lead PI Country

USA

Title of project or programme

Highly evolved brain circuits in primates: molecular vulnerabilities for disease

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NIH (NIA)

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30/09/2013

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4

The project/programme is most relevant to:

Neurodegenerative disease in general

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Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Dementia... Mental Health... Mental Illness... Neurodegenerative... Neurosciences... Schizophrenia

Research Abstract

DESCRIPTION (provided by applicant): Cognitive disorders such as Alzheimer's Disease (AD), Fronto-Temporal Dementia and schizophrenia are a tremendous burden on our society, as patients are often unable to care for themselves, and require extensive resources for many years. These disorders will be an even greater burden as our society grows older in the next decades. Current treatments are inadequate, and research in this arena continues to focus on mouse models. However, AD, schizophrenia, and related cognitive disorders primarily afflict the highly evolved association cortices which are poorly developed in mice, while the primary sensory cortices are little affected in these disorders. What makes the association cortices so vulnerable? And why are more basic cortical areas, such as the sensory cortices, more resistant to disease? These are fascinating evolutionary questions with immediate medical relevance. The proposed research will test the hypothesis that the highly evolved primate association cortices are more vulnerable to disease because they are regulated by Ca²⁺-cAMP signaling pathways in a fundamentally different manner than the evolutionarily older, sensory cortices, and that dysregulation of Ca²⁺-cAMP signaling following genetic or environmental insults predisposes these higher circuits to dysfunction and degeneration, e.g. through hyper-phosphorylation of tau. Our data have revealed that primate prefrontal association circuits contain high levels of cAMP-regulated K⁺ channels near their network connections that normally serve to gate inputs and provide mental flexibility. However, this process requires precise regulation, and even small insults to regulatory processes impair cognition and may increase risk for degeneration. A striking number of these proteins are genetically linked to schizophrenia, and show changes with advancing age. We hypothesize that primate cortical circuits will have differing sensitivities to Ca²⁺-cAMP signaling based on their evolutionary st

Lay Summary

The proposed research will determine why the brain regions afflicted in cognitive disorders such as Alzheimer's Disease and schizophrenia are so vulnerable to disease, and why other brain regions are resistant to degeneration. We hypothesize that recently evolved, molecular adaptations in our association cortex provide mental flexibility for high order cognitive operations, but may also render these brain circuits especially vulnerable to genetic and environmental insults. Understanding these fundamental differences may provide a new strategy for disease prevention and treatment.

Further information available at:

Types:

Investments > €500k

Member States:

United States of America

Diseases:

Neurodegenerative disease in general

Years:

2016

Database Categories:

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