

Regulation of striatal acetylcholine transmission by cholinergic interneurons

<https://neurodegenerationresearch.eu/survey/regulation-of-striatal-acetylcholine-transmission-by-cholinergic-interneurons/>

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Country

USA

Title of project or programme

Regulation of striatal acetylcholine transmission by cholinergic interneurons

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 1,240,554.13

Start date of award

15/01/2016

Total duration of award in years

4

The project/programme is most relevant to:

Huntington's disease

Keywords

Acetylcholine, cholinergic, Interneurons, Corpus striatum structure, Muscarinic Acetylcholine Receptor

Research Abstract

? DESCRIPTION (provided by applicant): The striatum is central to motivated behaviors and

goal-directed actions. Neuromodulation by acetylcholine (ACh) plays a major role in regulating striatal circuits and resulting behaviors. ACh levels within the striatum are the highest in the CNS. Cholinergic transmission is involved in multiple basal ganglia based functions including the control of voluntary movement, motor and associative learning, as well as reward. Dysfunctions in acetylcholine (ACh) signaling in the striatum are associated with a variety of neurological movement disorders including Parkinson's disease, Huntington's disease, and dystonia. Identifying how these dysfunctions occur is limited by a lack of understanding of the basic mechanisms of cholinergic transmission. While both nicotinic and muscarinic receptors are expressed in the striatum, ACh does not directly evoke post-synaptic events at most synapses that can be detected with conventional electrophysiological approaches. Instead cholinergic receptors modulate striatal inputs or indirectly alter the excitability of post-synaptic neurons through multistep intracellular cascades. To overcome the lack of direct readout of cholinergic transmission at muscarinic synapses, this proposal will use a novel approach to directly measure muscarinic receptor activation in medium spiny neurons of the striatum. By using the endogenous muscarinic receptor to detect the synaptic release of ACh in the striatum, this proposal will define how muscarinic receptors in striatal output neurons encode firing patterns of cholinergic interneurons, identify the role of glutamate co-release in shaping muscarinic transmission, and identify how neuromodulatory striatonigral inputs regulate ACh output. The proposed studies are expected to be significant in that they have the potential to be the first examination of a muscarinic mediated synaptic event in the striatum driven by the release of ACh from the firing of cholinergic interneurons. Insights into the specific mechanisms that regulate cholinergic transmission under physiological conditions are expected to directly lead to a testable hypothesis regarding the dysregulations in this system that occur in basal ganglia based movement disorders.

Lay Summary

PUBLIC HEALTH RELEVANCE: Neuromodulation by acetylcholine (ACh) plays a major role in regulating striatal circuits and downstream resulting behaviors. Alterations in cholinergic transmission in the striatum underlie numerous neurological diseases. A better understanding of the events linking acetylcholine release to its physiological actions will be significant as it has the potential to direct new strategies for the treatment of movement based neurological disorders.

Further information available at:

Types:

Investments > €500k

Member States:

United States of America

Diseases:

Huntington's disease

Years:

2016

Database Categories:

N/A

Database Tags:

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