Neuronal regulation of mitochondrial dynamics in models of Parkinsons disease.

https://neurodegenerationresearch.eu/survey/neuronal-regulation-of-mitochondrial-dynamics-in-models-of-parkinsons-disease/

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Neuronal regulation of mitochondrial dynamics in models of Parkinsons disease.

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1

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

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Parkinson Disease, Mitochondria, Neurons, neurotoxic, Regulation

Research Abstract

DESCRIPTION (provided by applicant): Evidence suggests that abnormalities in dynamic properties of mitochondria (fission, fusion, transport, biogenesis, and mitophagy) play a critical

role in Parkinson’s disease (PD) neuropathogenesis. These dynamic processes are necessary for maintenance of functional mitochondria and mitochondrial DNA, distribution of mitochondria to synapses, energy production, cell death mechanisms, and proper synaptic development and function. Mitochondrial dynamics are particularly critical to neurons, and the vulnerable neurons in PD may be especially dependent on these processes. Both genetic and environmental toxin-related models of PD have been linked to dysregulation of mitochondrial dynamics, but less is known about these processes in neurons. We and others have found differences in regulation of mitochondrial dynamics in neurons and have found that differences in neuronal bioenergetics may at least in part be responsible, suggesting the metabolic state of the cell is important. In addition, we found early alterations in mitochondrial dynamics in neurons in a chronic neurotoxic PD-relevant model, and we hypothesize that these changes are involved in early neuropathology in PD, and thus, are potential new targets for neuroprotective therapies. Thus, there is a critical need to understand neuron-specific regulation of mitochondrial dynamics and how this is altered in PD. We propose studies that will expand on our initial findings to better characterize alterations in neuronal mitochondrial fission, fusion, biogenesis and mitophagy in both PD-relevant genetic and chronic environmental models, and begin to elucidate possible mechanisms. Importantly, we will also expand our work to include imaging and quantification of mitochondrial dynamics directly, in dopamine (DA) neurons, in an innovative, living vertebrate PD model, thus better dissecting the role of mitochondrial dynamics in early neuropathology in PD. These studies will provide important information on neuronal regulation of mitochondrial dynamics, as well as provide a better understanding of the integrated role of mitochondrial dynamics in PD.

Lay Summary
This research is focused on understanding the role of changes in mitochondrial homeostasis in the neurodegeneration of Parkinson’s disease. Because it is aimed at elucidating potential underlying mechanisms involved early in pathogenesis, it may identify new targets for neuroprotection in Parkinson’s disease.

Further information available at:

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Investments > €500k

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