Targeting NMDA receptor dysfunctions in Parkinson´s disease

https://neurodegenerationresearch.eu/survey/targeting-nmda-receptor-dysfunctions-in-parkinsons-disease/

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Country

Sweden

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Targeting NMDA receptor dysfunctions in Parkinson´s disease

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Swedish Research Council

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3

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Research Abstract
Current therapeutic approaches for the treatment of Parkinson’s disease (PD) are associated with severe side effects or loss of efficacy in the late stages of the disease. It is therefore essential to develop improved and more effective tools, with reduced side effects, for the treatment of PD. Our recent studies propose the GluN2D subunit of NMDA receptors as a potential novel target for the development of antiparkinsonian compounds. Thus, one of the consequences of striatal dopamine depletion includes a switch between GluN2B and GluN2D in projection neurons and loss of GluN2D in cholinergic interneurons of the striatum. We will further determine the functions and dysfunctions of NMDARs, in particular those containing GluN2D, in the striatum and in dopaminergic neurons in two models of PD, i.e. the 6-OHDA

lesioned mouse and the DAT-Nurr1 KO mouse in which the transcription factor Nurr1 is ablated in adult dopaminergic neurons. We will also examine whether deletion of GluN2D in specific neuronal populations (i.e. cholinergic interneurons, medium spiny neurons, dopaminergic neurons) mimic or exacerbate neurophysiological, neurochemical and motor impairments in experimental Parkinsonism. We will also identify means to rescue impairments in mouse models of PD, and suggest potential disease modifying strategies. These studies will allow determining whether manipulations of GluN2D-containing NMDARs could be of therapeutic benefit in the management of symptoms of PD.

Further information available at:

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Investments < €500k

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