

Testing predictions of quantitative models of dopamine signals in different stages of Parkinson's disease.

<https://www.neurodegenerationresearch.eu/survey/testing-predictions-of-quantitative-models-of-dopamine-signals-in-different-stages-of-parkinsons-disease/>

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Country

Denmark

Title of project or programme

Testing predictions of quantitative models of dopamine signals in different stages of Parkinson's disease.

Source of funding information

Lundbeckfonden

Total sum awarded (Euro)

€ 242,150

Start date of award

01/05/2014

Total duration of award in years

2

Keywords

Research Abstract

Recent computational models have identified a dual effect of DA denervation in striatum, the condition leading to Parkinson's Disease (Jakob Dreyer, unpublished). Here we found that geometrical aspects of the DA lesion in striatum play a determining role in shaping the post synaptic response of the DA signal. The DA signal is radically different and opposite in partially denervated areas compared to fully denervated regions. Therefore the intuitive consensus

model of Parkinson's disease (Figure 1A) does not describe early and presymptomatic phases of the disease and fits only partially in the late stage. In early stages of PD, DA tone is conserved by passive stabilization and denervation leads to loss of phasic high and low DA levels and 'paradoxical' D2 hyperactivity. Based on an analysis of underlying physics of DA signals I propose a theory of DA signals in Parkinson's disease (The Swiss Cheese Theory, SCT) and a post synaptic compensatory mechanism (Phasic Amplitude Compensation, PAC). Combination of SCT and PAC leads to super sensitivity of D1 and D2 receptors in partly innervated tissue and reduced D2 expression in fully depleted areas. The theory predicts the full behavioral spectrum of 6-OHDA lesioned animals including 'paradoxical' contraversive rotations in early stage when challenged with low dose psychostimulants, apomorphine induced contraversive rotations and amphetamine induced ipsilateral rotations. The project here aims at experimental verifications of theoretical predictions and development of a large scale computational model with the long term goal of analyzing DA signaling in human Parkinson's patients.

Further information available at:

Types:

Investments < €500k

Member States:

Denmark

Diseases:

N/A

Years:

2016

Database Categories:

N/A

Database Tags:

N/A