Time course assessment following bilateral and unilateral-dual inoculation of α-synuclein preformed fibrils in C57Bl/6 mice

Presenting author: Irene Morganstern, irene.morganstern@psychogenics.com

Author and co-authors' details: Daniel Havas[1], Christina Torturo[1], Smriti Mongia[1], Kristina Kovacovicova[1], E. Tsika[2], Irene Morganstern[1], Sylvie Ramboz[1]

Affiliation details:

[1]PsychoGenics Inc, Paramus, NJ, USA

[2]: AC Immune SA, Lausanne, Switzerland

We sought to build on previously published α-synuclein Parkinson's disease models by examining the pathology development over time post-inoculation of mouse α-synuclein preformed fibrils [PFF] into the striatum of both hemispheres, or into the striatum and substantia nigra of one hemisphere, of C57Bl6/J WT mice. PFF were inoculated via stereotaxic surgery into bilateral mouse striatum, or unilateral dual mouse striatum-substantia nigra. Behavior and immunohistochemistry were assessed 30, 60, and 90 days post-inoculation (DPI).

Bilateral striatal PFF-injected mice displayed strong Lewy-body-like pathology with hyperphosphorylated α-synuclein aggregates spreading from the striatum to the substantia nigra (SN), amygdala and layer IV of the neocortex. Stronger pathology was seen in striatum of bilaterally inoculated mice at 30 DPI and dropping by 50% at 60 DPI onwards. In the SN, the drop occurred at later DPI reflecting loss of TH+ dopaminergic neurons in this region. In contrast, multimeric α-synuclein increased from 30 to 90 DPI, while not altered in the unilateral model at 90 DPI. TH+ neuronal loss was observed in the SN of bilaterally injected mice at 60 DPI, 30 days earlier than the unilateral model. No significant motor deficits were observed except a significant increase in the wire hang latency to fall in the bilaterally striatal PFF-injected mice.

Inoculating PFF into the striatum bilaterally led to a substantial enhancement of pathology to both hemispheres with no major impact on the assessed motor behavior readouts. Concluding remarks are pending additional data analysis from the unilateral, dual striatal-substantia nigral stereotaxic inoculation animal group. Further investigations and analysis are required to characterize this model for testing disease-modifying therapies for Parkinson's disease.