Glycation modulates glutamatergic signalling and exacerbates Parkinson’s disease-like phenotypes

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SYNUCLEINOPATHIES

- Parkinson’s disease
- Dementia with Lewy bodies
- Mostly idiopathic
- Incurable

Type-II diabetes mellitus is a risk factor for Parkinson’s disease

GLYCATION potentiates αSyn toxicity, aggregation, and impairs its clearance

GLYCATION induces dopaminergic neuronal loss and αSyn oligomerization

HYPOTHESIS

Glycation-induced dysfunction of neuronal pathways might be an underlying molecular cause of synucleinopathies

Experimental design

Wild-type littermates (WT) and Thy1-αSyn transgenic mice received an intrastriatal/intracerebral (IS/IC) injection of methylglyoxal (MGO) or vehicle (PBS) at 16 weeks of age. Behavioral testing started 4 weeks post-surgery. Post-mortem studies included histological, SWATH-MS, and biochemical analyses.

MGO potentiates motor, cognitive, olfactory and colonic disturbances in Thy1-αSyn mice

MGO treatment induces neurodegeneration in Thy1-aSyn mice

Proteomic analysis: protein alterations quantified in the midbrain of MGO-treated Thy1-αSyn mice that are not modulated by MGO-treatment of αSyn-expression alone.

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MGO dysregulates glutamatergic signalling in the midbrain

Glycation exacerbates motor, cognitive and olfactory deficits in Thy1-αSyn mice, that show accumulation of αSyn and AGEs and exacerbated glutamatergic signalling in the MIDBRAIN

FUNDING

References

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