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α -Synuclein-Induced Increase in DOPA Decarboxylase-Expressing Cells in the Retina

Teo Sällberg¹, Valentina Cesaroni², Jessica Santiago¹, Angela Censi-Nilsson³, Malin Wennström¹.

1. Clinical Memory Research Unit, Department of Clinical Sciences Malmö, Lund University, Malmö, Sweden.

2. Diabetes and Brain Function Unit, Department of Experimental Medical Science, Lund University, Lund, Sweden.

3. Basal Ganglia Pathophysiology Unit, Department of Experimental Medical Science, Lund University, Lund, Sweden.



Key findings: Intracranial mPFF injection induces α -synuclein propagation to the retina. DDC+ cell numbers increase in response to retinal α -synuclein accumulation, independently of TH+ cell loss..

Background

Parkinson's disease (PD) is marked by the progressive loss of dopaminergic neurons in the substantia nigra, but growing evidence shows that pathology also affects the retina, making it a promising site for non-invasive biomarker discovery. While tyrosine hydroxylase (TH) and dopa decarboxylase (DDC) together catalyze the two key steps of retinal dopamine synthesis, how these enzymes are altered in PD remains largely unknown.

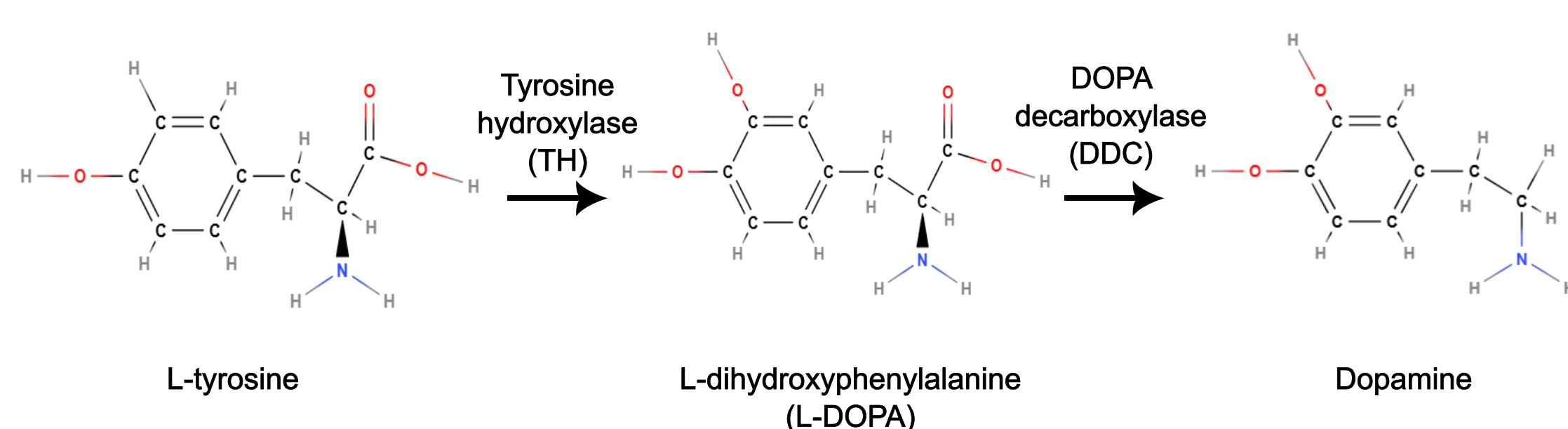


Figure 1. Overview of the dopamine synthesis pathway, highlighting the enzyme TH and DDC.

Methods

Wild-type mice were bilaterally injected with α -synuclein preformed fibrils (mPFFs) (n=7) or saline as controls (n=8). Retinas were collected and processed as either flat mounts or cross-sections. Immunofluorescence staining was performed for phosphorylated α -synuclein (pS129- α -syn), TH, and DDC to assess retinal α -syn pathology and dopaminergic alterations.

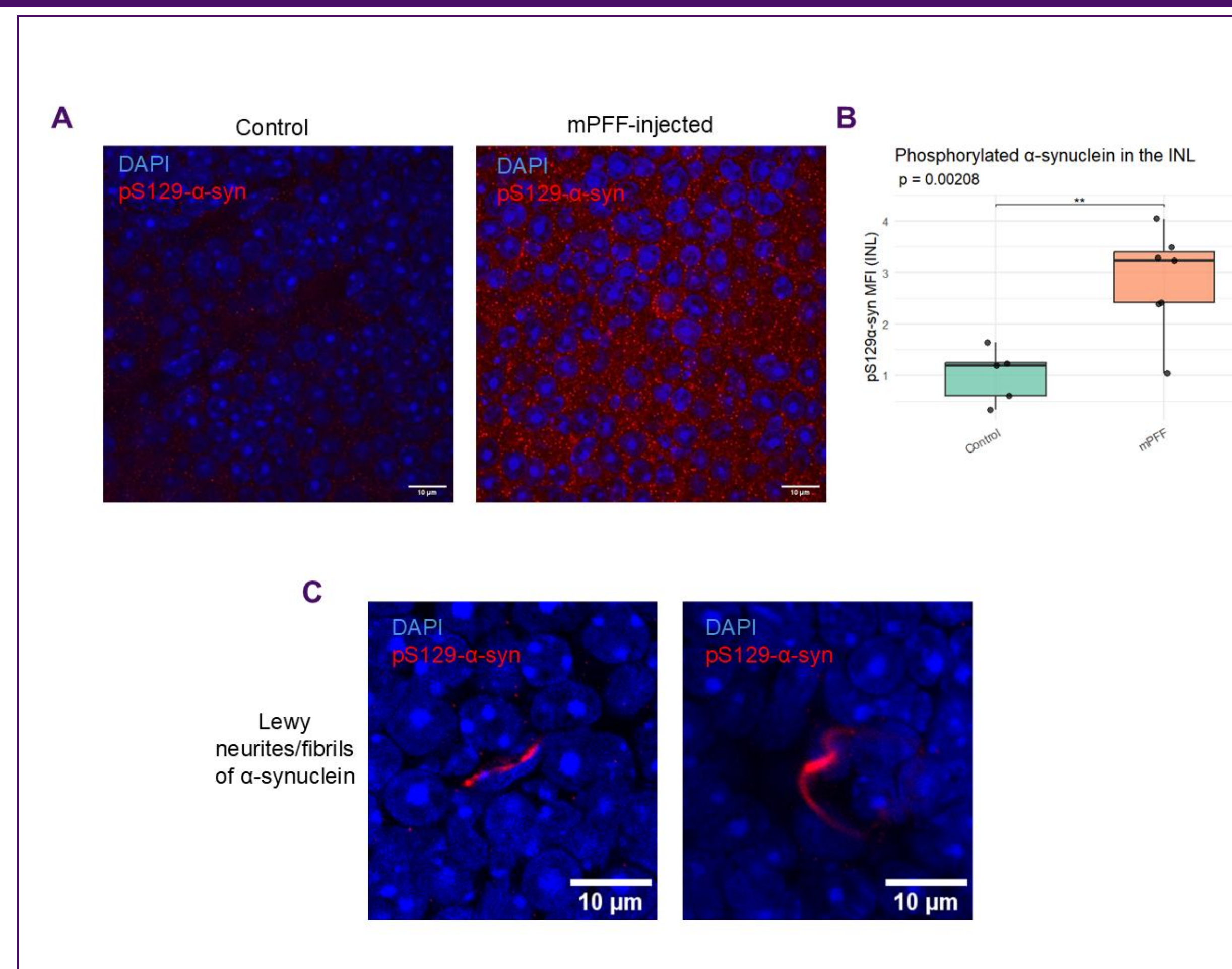


Figure 2. α -Synuclein accumulation in the retina following intracranial mPFF injection.

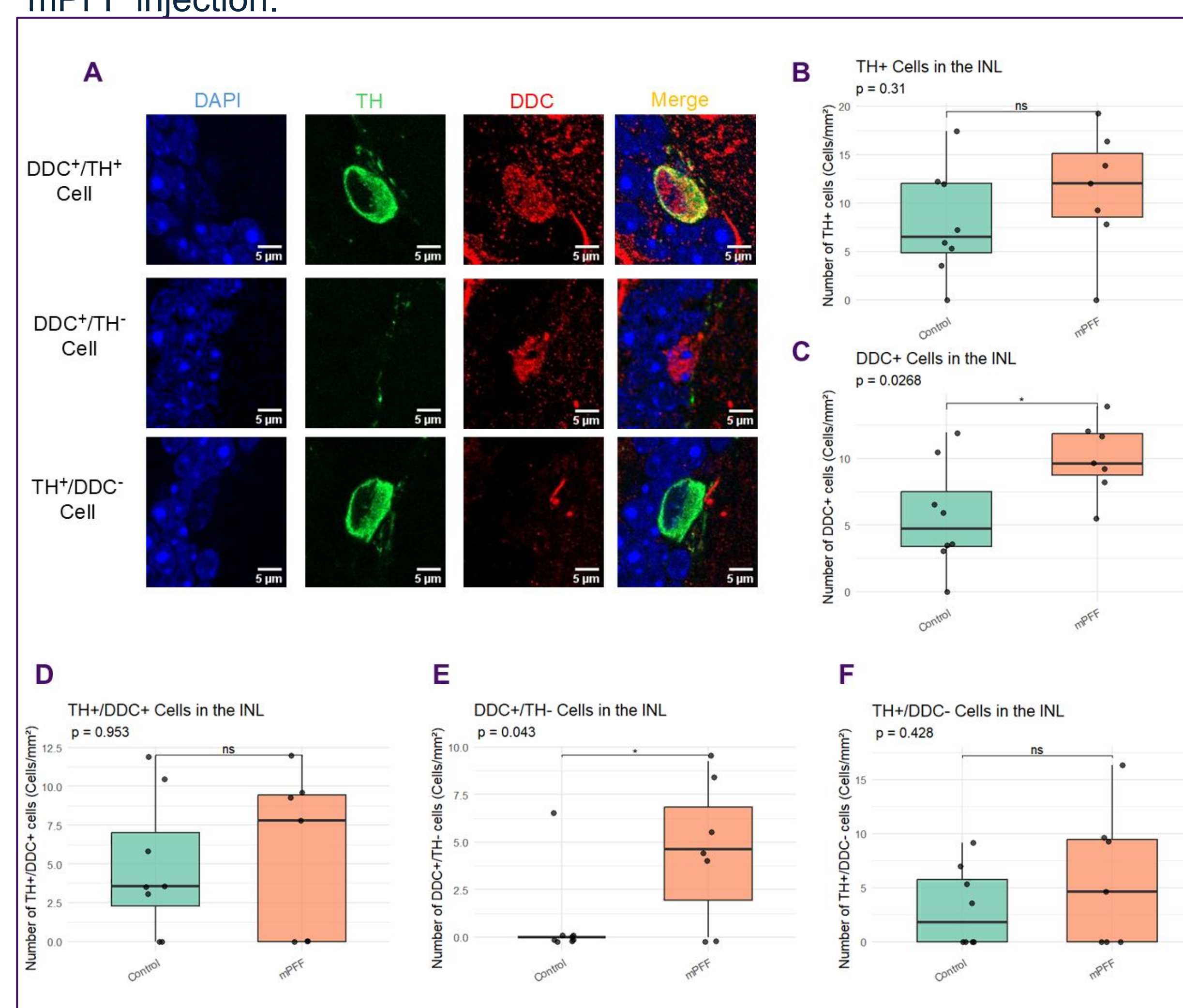


Figure 3. TH/DDC phenotypic distribution in the retina following intracranial mPFF injection.

Results

Immunofluorescent analysis of retinal tissue revealed increased accumulation of phosphorylated α -synuclein, indicating propagation of pathological α -synuclein to the retina. Concomitantly, we observed a significant increase in the number of DDC-positive cells, the enzyme catalyzing the final step in dopamine synthesis. In contrast, the number of TH-positive cells was not significantly altered.

Conclusion

Our findings indicate that intracranially injected α -synuclein propagates to the retina and is associated with an increased population of DDC-expressing cells, independent of dopaminergic cell loss. This suggests a potential compensatory retinal response to dopamine deficiency and highlights the retina as a promising site for studying PD-related neurodegeneration.

References

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