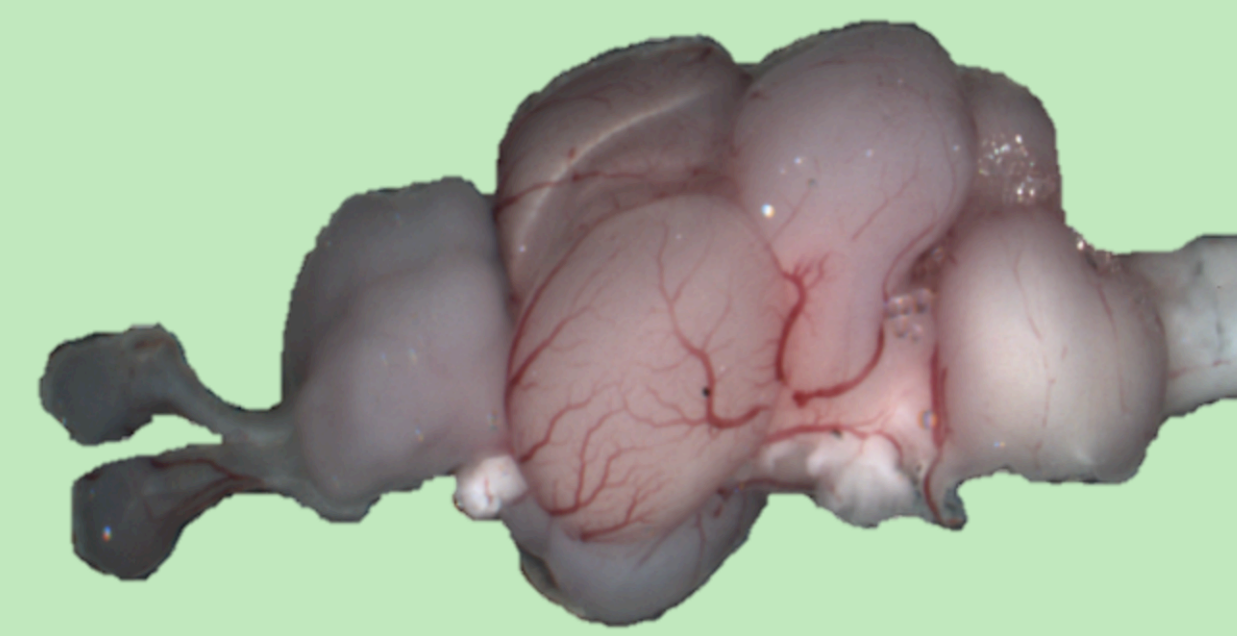




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Neuroregenerative ability of fish brain after neurotoxin-induced Parkinson's disease



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Abstract

Due to a low amount of precursor cells, the adult human brain has difficulty regenerating damaged dopamine neurons which leads to neurodegenerative diseases like Parkinson's syndrome. Fish have a strong capacity to regenerate neurons due to their abundance of radial glial cells. These neuronal precursor cells are aromatase-positive. The objective of the present study is to determine if neurogenesis, after neurodegeneration induced by the neurotoxin MPTP, is aromatase-dependant. Immunohistochemistry was used to discern the effects of exposure to MPTP and Fadzozole and the potential influences on dopamine neurons. The fish showed increases of glial fibrillary acidic protein in RGCs and decreases of tyrosine hydroxylase, indicating induction of Parkinson's syndrome and activation of radial glial cell functions. Degeneration of dopamine neurons is potentially aromatase-dependent. This neuroanatomical data will help us better understand the mechanisms underlying neurogenesis and potential therapy for Parkinson's disease.

Introduction

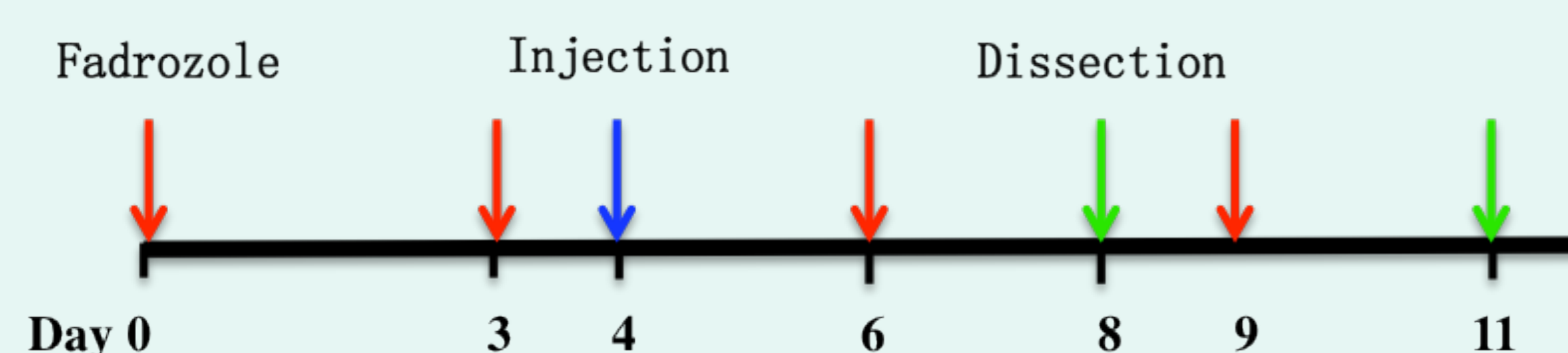


- Neurogenesis in humans is low; therefore neurodegeneration causes incurable diseases such as Parkinson's syndrome, generated by the loss of dopaminergic neurons [1].
- Sufficient amounts of neuronal precursor cells may reverse the effects of neurodegenerative diseases.
- Radial glial cells are aromatase-positive precursor cells that adult fish have in sizeable quantities [2].
- Since RGCs are aromatase-positive, neurogenesis of dopamine neurons may be aromatase-dependant.

Methods



- Treat female goldfish with MPTP (50µg/g body weight, i.p. injection) and/or fadzozole (50µg/L, dissolved in water) according to the following timeline.
- Dissect, then fix, embed and section brain tissue (20µM).
- Perform immunofluorescence with anti-GFAP and anti-TH primary antibodies and reveal staining with donkey anti-rabbit Alexa fluor 488 and goat anti-mouse Alexa fluor 596 secondary antibodies.
- Mount slides with anti-fading medium with DAPI.



Results

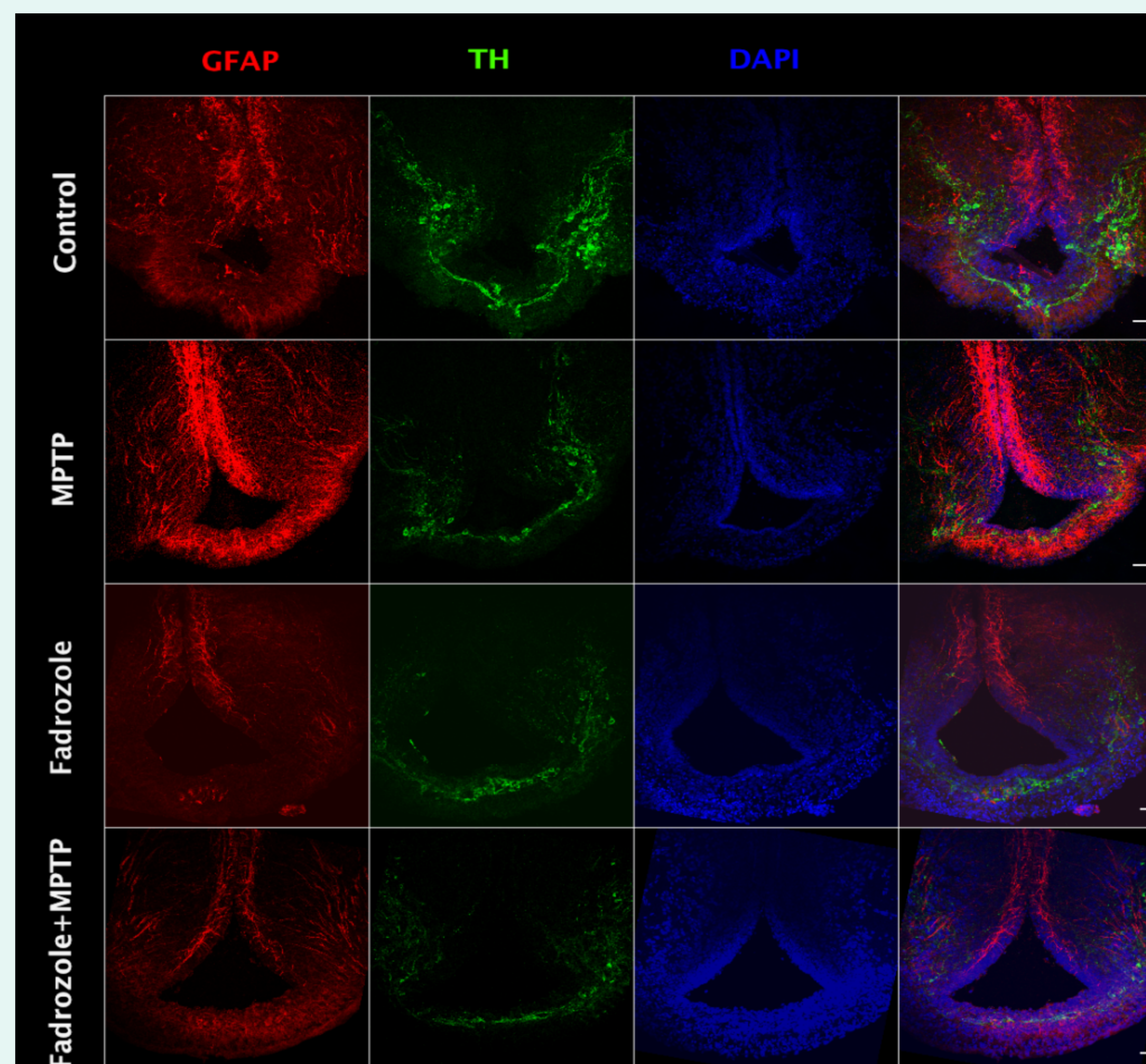


Fig. 1 Double fluorescence detection of glial fibrillary acidic protein and tyrosine hydroxylase (TH; green) in female goldfish ventral telecephalic area 4 days after MPTP injection and 8 days after fadzozole exposure. The confocal image shows RGCs marked by GFAP (red) located along the ventricular surface. Catecholaminergic neurons marked by TH are close to RGCs. The nuclear stain DAPI (blue) is also shown. Scale bar=10 µm.

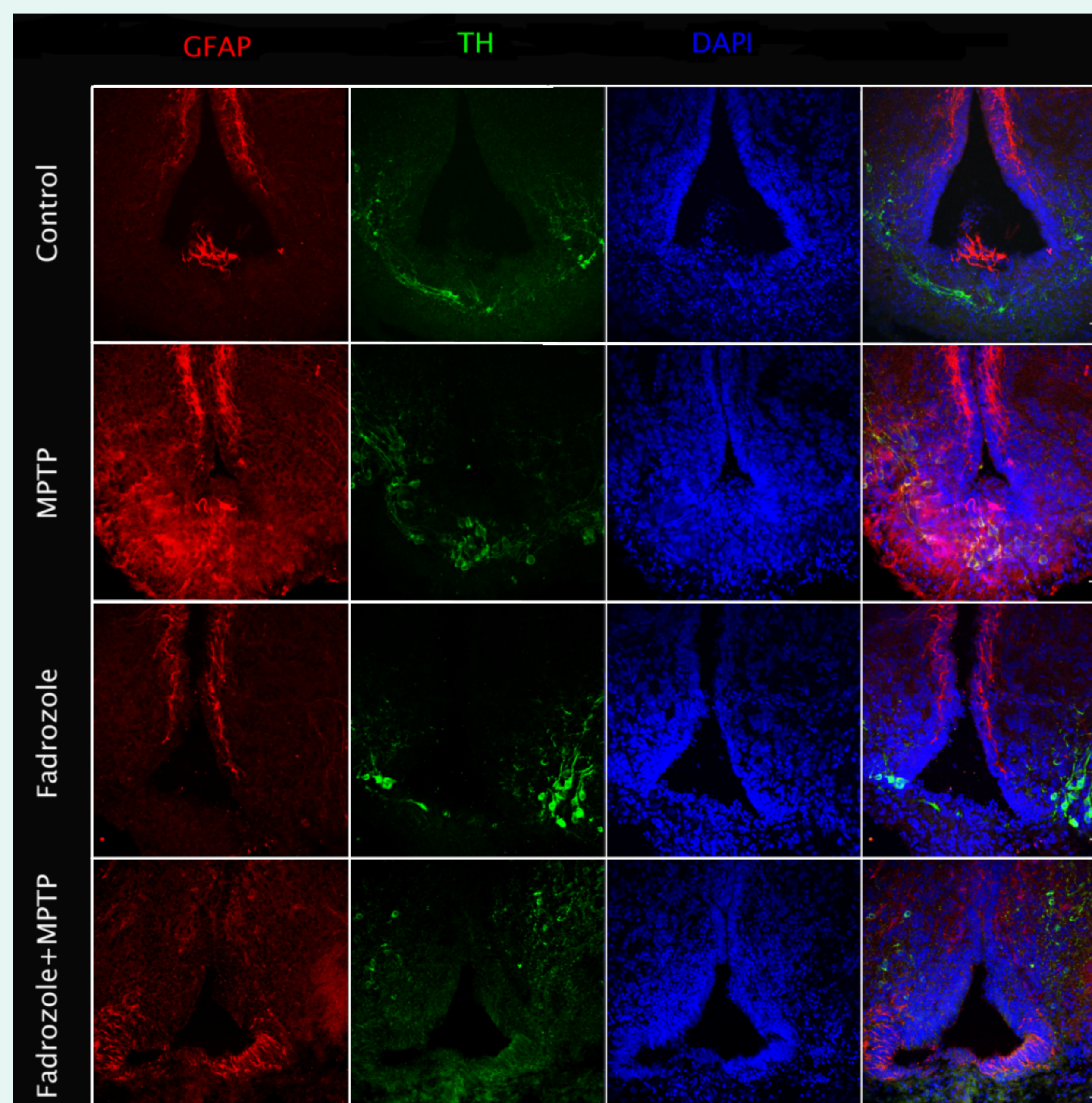


Fig. 2. Double fluorescence detection of glial fibrillary acidic protein (GFAP; red) and tyrosine hydroxylase (TH; green) in female goldfish ventral telecephalic area 7 days after MPTP injection and 11 days after fadzozole exposure. The confocal image shows RGCs marked by GFAP located along the ventricular surface. Catecholaminergic neurons marked by TH are close to RGCs. The nuclear stain DAPI (blue) is also shown. Scale bar=10 µm.

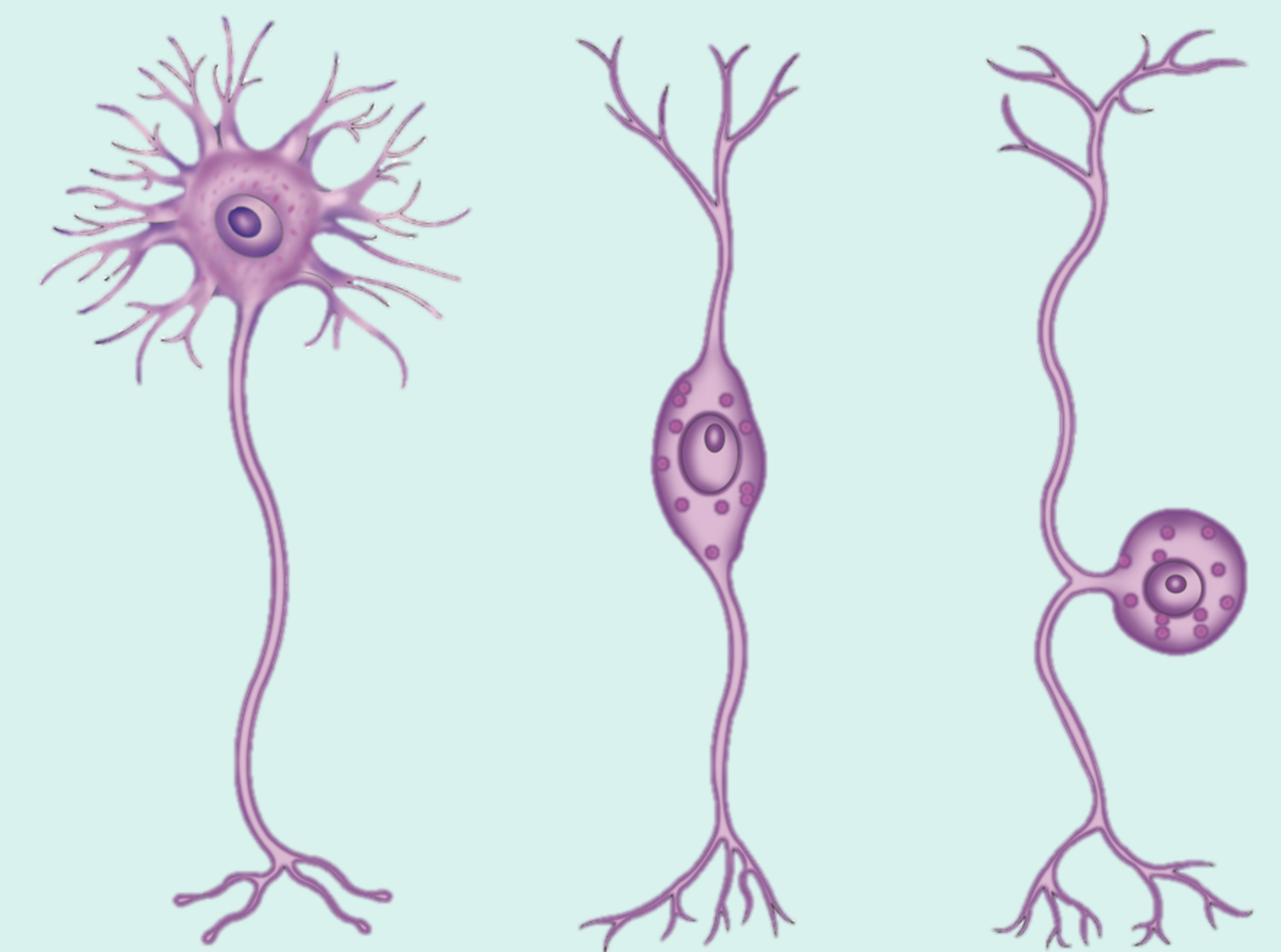
Quantitative Results

		Control	MPTP	Fadzozole	Fadzozole +MPTP
DAY4	GFAP	++	+++	++	++
	TH	++	+	++	+
DAY7	GFAP	++	+++	++	+
	TH	++	++	++	++

Table.1 Semi-quantitative analysis of immunofluorescence images (n=3).

Conclusions

- MPTP successfully induced Parkinson's-like symptoms and activated radial glial cell functions in female goldfish.
- Much less activity in RGCs when Fadzozole exposure is combined with MPTP exposure.
- Neurogenesis of dopaminergic neurons is potentially aromatase-dependent.
- Further research into the matter may lead to potential cures for Parkinson's syndrome.



Bibliography

1. GARCIA -VERDUGO *et al.* 2002. Brain Research Bulletin. Vol. 57, No. 6, pp. 765-775
2. MENUET A *et al.* 2005. The Journal of Comparative Neurology. 485:304-320.

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