Eye movement deficits in a zebrafish model of Parkinson's disease

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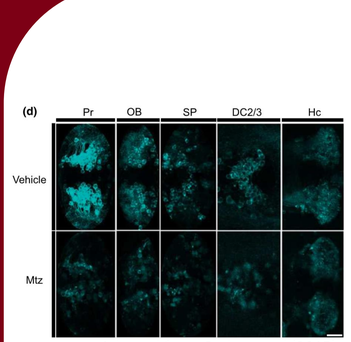
Introduction

Parkinson's Disease is characterized by the loss of dopaminergic neurons in the substantia nigra. These DA neurons project to various nuclei of the basal ganglia to shape motor control. Some Parkinson's Disease (PD) patients show impaired visual function related to a selection of eye movements but show heightened reflexive eye movements. However why the loss of DA neurons leads to these deficits in eye movements is not clear. In this study we used the optokinetic response of larval zebrafish to explore eye movement deficits in detail.

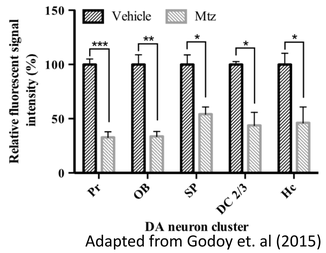
Basal Ganglia → DA → Superior Colliculus → Saccade

Methods & Materials

To generate a PD model of zebrafish in which DA neurons are lost, dat:CFR-NTR transgenic fish were raised in a metronidazole (MTZ) infused environment. MTZ is converted by NTR into a cytotoxic product, and our previous work has shown that it leads to the selective loss of DA neurons[1]. The optokinetic reflex was tested on groups with ablated dopaminergic neurons and an untreated group.

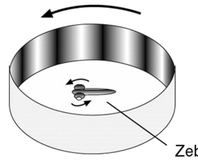


Adapted from Godoy et. al (2015)



Adapted from Godoy et. al (2015)

The optokinetic response (OKR)



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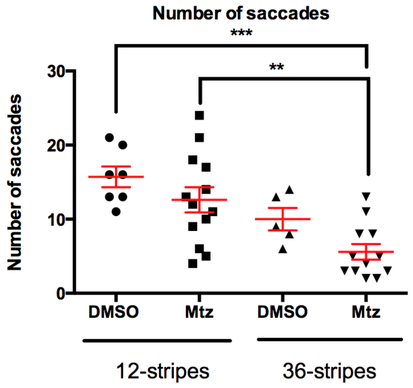

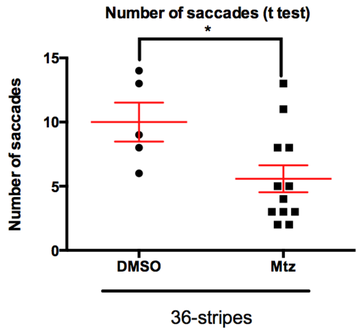

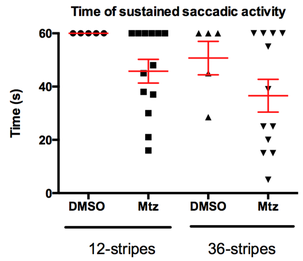

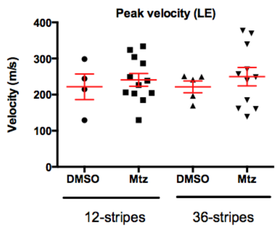

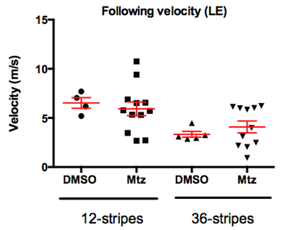

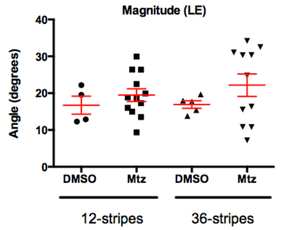

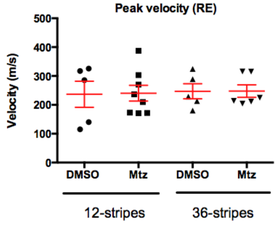

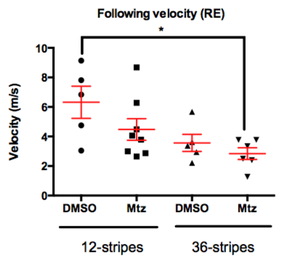

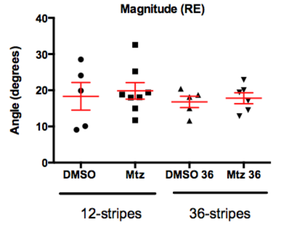

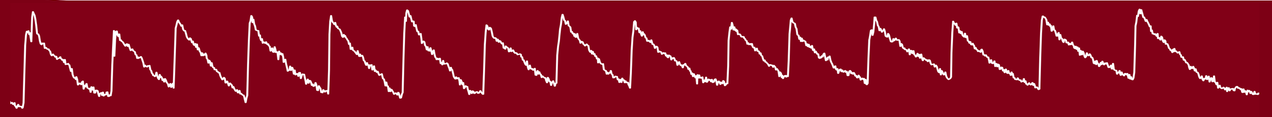

Conclusions

With this method, we found that there are significant differences between the treated and untreated animals. More specifically, the number of saccades in the 36-stripe test between the treated and untreated fish is significantly different, however, all other parameters (peak velocity, following velocity, and magnitude) were similar. This suggests that dopamine plays a role in saccade initiation at low spatial frequencies. In conclusion, this work suggests that zebrafish can be used to study how the loss of DA affects eye movements in Parkinson's Disease.

Stimulus → Processing → Initiation → Execution

Loss of DA

References

1. Godoy, R., Noble, S., Yoon, K., Anisman, H., Ekker, M. (2015). J. Neurochem. 135(2): 249-60.
2. Roeser T., Baier H. (2003) J. Neurosci. 23(9), 3726–3734

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