Testing Purkinje Cell Role in Stimulation of VOR Adaptation

B Davis, D Garcia, J Lewis, C Worthington, T Stay
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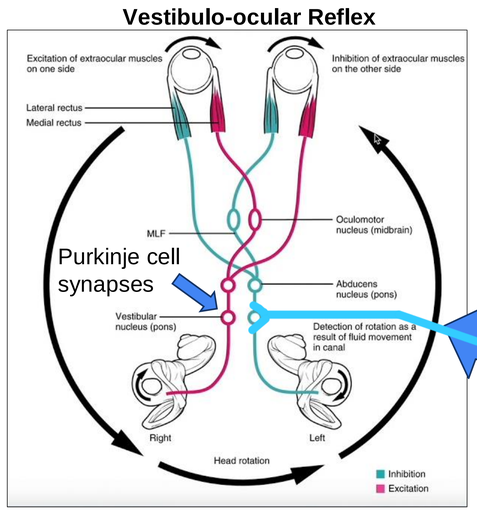
References

Background

The vestibulo-ocular reflex (VOR) is coordinated eye movement to maintain a stable gaze during head rotation. This reflex can be adapted through behavioral training by using repeated head movements and shifting visual stimuli.

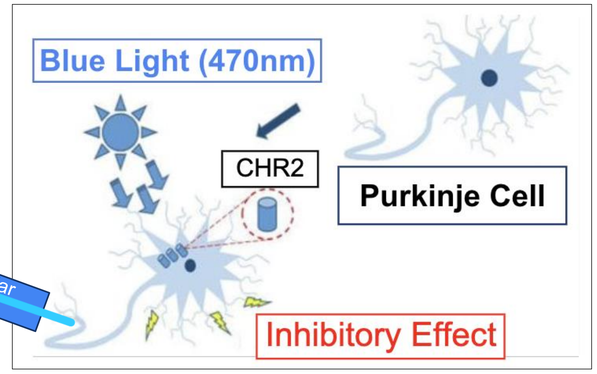
Through previous research (Kimpo et al., 2014) has implicated cerebellar output as critical to VOR adaptation, it is unclear whether Purkinje cell output alone is sufficient for driving reflex adaptation.

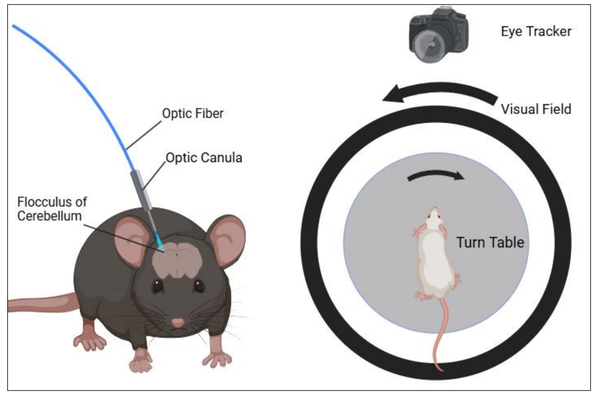
Our primary question is if Purkinje cell stimulation is sufficient to drive the adaptation of the VOR when paired with either vestibular or visual stimuli. Stimuli include head movement or visual motion cues such as a rotating drum around the mouse. If Purkinje cell stimulation when combined with one of these two stimuli is sufficient for changing VOR gain, we would see increased long term gain during optogenetic stimulation. If Purkinje cell stimulation is insufficient, we could see results where stimulation leads to short-term learning but no long-term retention occurs. It is also possible that no learning occurs.



Methods

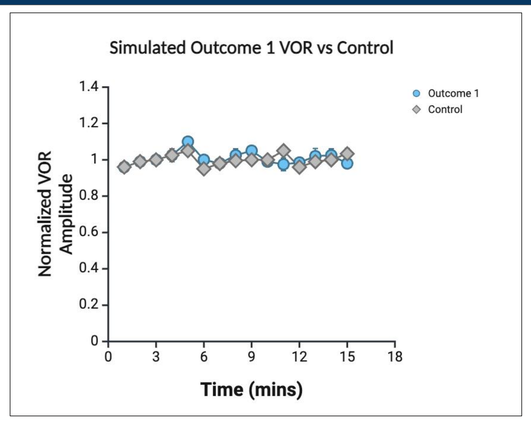
We will express channelrhodopsin (ChR2) in murine Purkinje cells, which depolarizes to 470nm light. We will insert an optic fiber into the flocculus of our ChR2 mice which will allow us to stimulate the Purkinje cells with pulses of light.

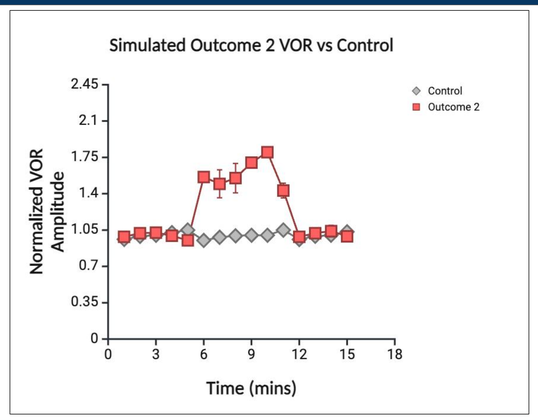


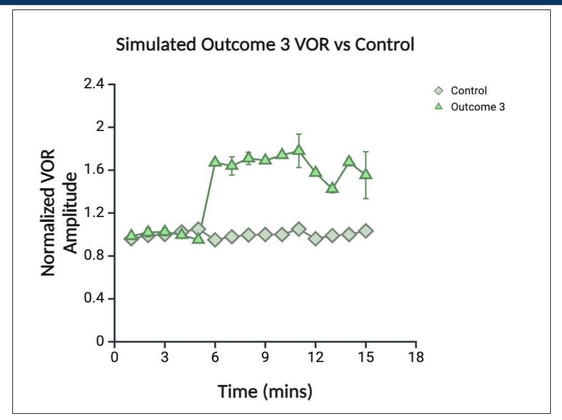


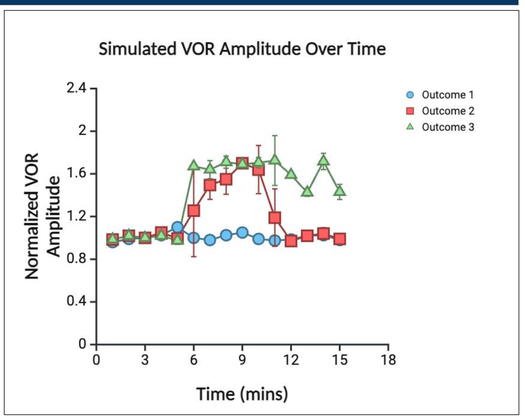
We will pulse 470nm light for 10ms bursts (1ms on, 1ms off), repeated 20 times centered on peak ipsiversive head or visual velocity, over the course of 15 minutes.

Simulated Data









Potential Results and Proposed Follow-Up Research

Stimulation has no result

As displayed, the VOR gain (ratio of the change in eye angle to the change in head angle) begins at a baseline of 1, does not increase during training, and then remains at that level after, indicating no change.

The most probable cause for no VOR gain could be due to inadequate expression of ChR2 gene in the Purkinje cells. Other potential causes include excessive animal stress levels or improper placement of the optic canula.

We would test this through post hoc histology and potentially measuring blood corticosterone.

Stimulation has short term VOR effect

The baseline VOR gain increases during training, but no increase is sustained through long-term testing.

A possible result could be temporary VOR gain. VOR gain that is transient could be explained by insufficient Purkinje cell output to the VOR circuit itself when coupled with vestibular and visual input. In this case, stimulation of Purkinje cells is not enough to drive lasting adaptation.

We could increase the length of time or light intensity of the stimulus to see whether that affects long-term adaptation.

Stimulation drives long term VOR gain

Pretraining levels start at a baseline and then increase during training. Post-training indicates long term VOR gain adaptation.

This result would indicate that Purkinje cells impact short and long-term VOR gain through their stimulation.

Moving forward, an inhibition of Purkinje cells in future experiments could help to show their necessity for VOR gain. We could also test sufficiency of Purkinje cell output for VOR decrease adaptation.

Special Acknowledgments

LARC care staff for maintenance of mice

BYU Department of Psychology

Feedback

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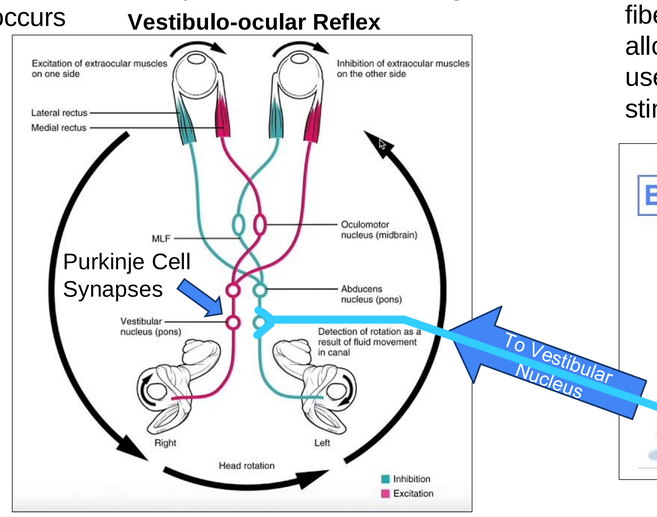
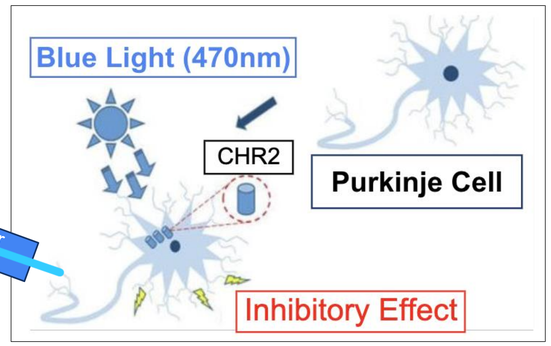
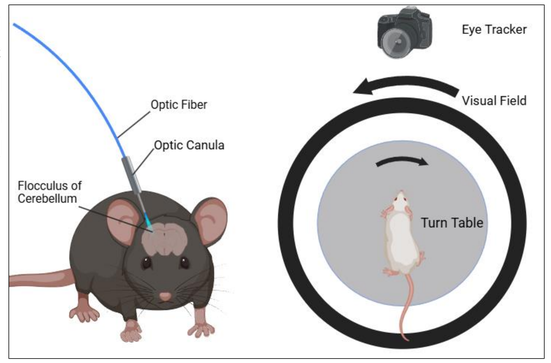
Our primary question is if Purkinje cell stimulation is sufficient to drive the adaptation of the VOR when paired with various vestibular and visual stimuli. Stimuli include head movement or visual motion cues such as a rotating drum around the mouse. If Purkinje cell stimulation when combined with these two stimuli is sufficient for VOR gain, we would see increased long term gain during optogenetic stimulation. If Purkinje cell stimulation is insufficient, we could see results where stimulation leads to short-term learning but no long-term retention occurs. It is also possible that no learning occurs



Methods

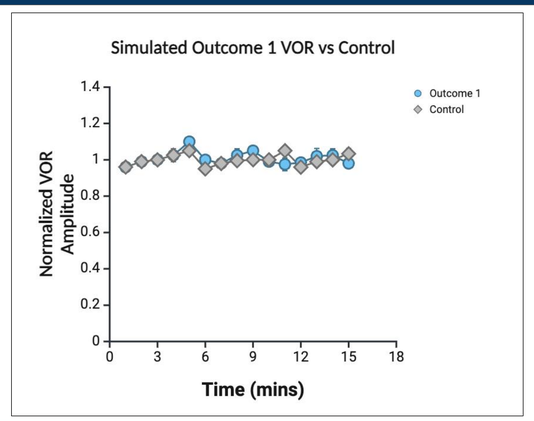
In genetically modified mice, the ChR2 cation channel activates the Purkinje cells when exposed to light of 470nm. We will insert an optic fiber into the flocculus of our ChR2 mice which will allow us to stimulate the Purkinje cells. We will use bursts of short short 4ms pulses during stimulation.

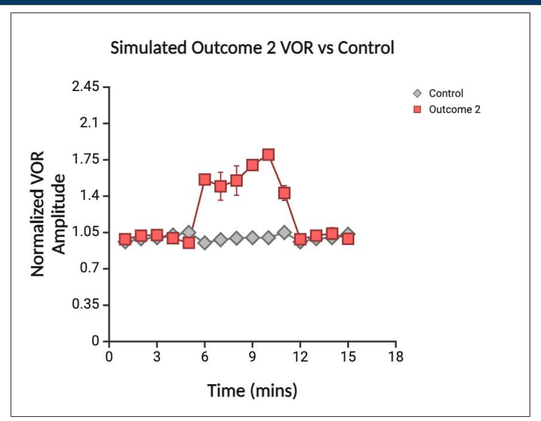


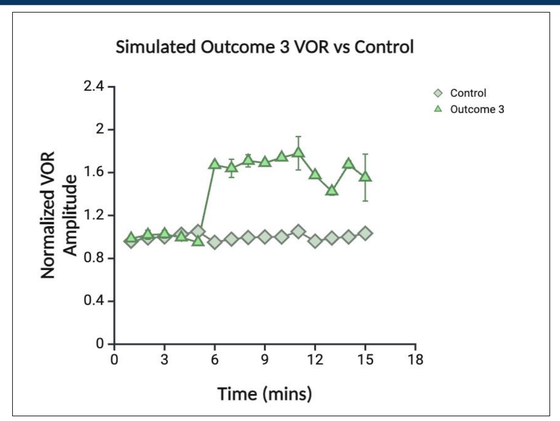


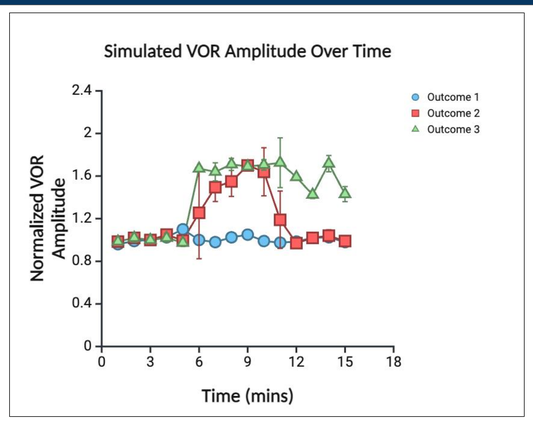
We will conduct behavioral experiments to deduce whether activation of Purkinje cells during visual and vestibular stimulation has long term effects on VOR gain by measuring eye movement during optogenetic stimulation.

Simulated Data









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Reference page

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