The Role of NMDA Receptor Activity in Retinal Ganglion Cell Dendrite Development

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Introduction

Background- Retinal ganglion cell dendrites undergo dramatic structural changes during development as they grow out into the inner plexiform layer, stratify, and form synapses with bipolar and amacrine cells.

Problem- Conflicting studies cannot agree whether or not retinal ganglion cell dendritic development is activity dependent.

Hypothesis- Activity-dependent dendritic development depends on ganglion cell subtype. We predict that the refining RGC subtype, JamB, requires glutamatergic activity for dendrite development.

Methods

- Model: JamB-CreER:YFP mice label OFF DS ganglion cells.
- Imaging: confocal microscopy of WT and Grin1-/- JamB-CreER:YFP retinal whole-mounts.
- Experimental treatments: 400 uM AP5 and 40 uM CNQX were injected intraocularly to block spontaneous glutamatergic activity before eye-opening. Dark-reared mice were housed in a dark box from P6 to P30.
- Analysis: Individual neurons were traced using NeuroLucida and analyzed with NeuroExplorer to measure dendrite length, protrusion number, and dendritic field area.

Results

JamB RGC dendritic development occurs in two phases

- Dendrites are 50 µm.
- Dendritic expansion requires glutamatergic activity.

Dendritic field consolidation is absent in NMDAR KO JamB RGCs

- NMDAR receptors drive dendritic expansion.
- NMDA receptors are required for JamB dendritic expansion.
- Blockade of synaptic activity mediated by glutamate receptor (GluR) selectively impairs the dendritic elongation of JamB RGCs.

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Summary

- JamB RGC dendritic development occurs in two phases, (1) dendrite elongation and field expansion and (2) elimination of dendritic protrusions and DF consolidation.
- Dendritic elongation requires glutamatergic activity in the retina.
- NMDA receptors on JamB RGCs are required for protrusion elimination, dendrite elongation, and DF expansion before eye-opening.
- NMDA receptors may be required for DF consolidation.
- Visual input drives DF consolidation.

References