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Functional Assembly of Accessory Optic System Circuitry Critical for Compensatory Eye Movements

Highlights

- Sema6A is expressed in On DSGCs innervating AOS brain targets
- Sema6A is required for the development of AOS axon trajectories
- PlexA2 and PlexA4 serve as attractive ligands for Sema6A^{+} On DSGCs
- PlexA2/A4-Sema6A reverse signaling facilitates compensatory eye movements

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In Brief

The molecular mechanisms that direct the development of the accessory optic system (AOS) are poorly understood. In this study, Sun et al. show that PlexA2/A4-Sema6A reverse signaling regulates the functional assembly of AOS connections critical for compensatory eye movements.

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Functional Assembly of Accessory Optic System Circuitry Critical for Compensatory Eye Movements

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SUMMARY

Accurate motion detection requires neural circuitry that compensates for global visual field motion. Select subtypes of retinal ganglion cells perceive image motion and connect to the accessory optic system (AOS) in the brain, which generates compensatory eye movements that stabilize images during slow visual field motion. Here, we show that the murine transmembrane semaphorin 6A (Sema6A) is expressed in a subset of On direction-selective ganglion cells (On DSGCs) and is required for retinorecipient axonal targeting to the medial terminal nucleus (MTN) of the AOS. Plexin A2 and A4, two Sema6A binding partners, are expressed in MTN cells, attract Sema6A$^+$ On DSGC axons, and mediate MTN targeting of Sema6A$^+$ RGC projections. Furthermore, Sema6A/Plexin-A2/A4 signaling is required for the functional output of the AOS. These data reveal molecular mechanisms underlying the assembly of AOS circuits critical for moving image perception.

INTRODUCTION

The detection of object motion is an essential visual system function mediated by direction-selective (DS) circuitry in the retina and in retinorecipient brain regions targeted by DS retinal ganglion cells (RGCs). In addition to tracking moving objects, a critical function served by visual system DS responses is the ability to compensate for global visual field motion. This can be caused by the observer's rapid head movements or by overall slow movement of the observer through the visual scene. Failure to execute image-stabilizing eye movements that compensate for self-induced global visual field motion results in blurred image perception. To prevent this, the accessory optic system (AOS) of the mammalian visual system and the vestibular system converge to direct oculomotor output critical for image stabilization (Simpson, 1984). The vestibular semicircular canals compensate for rapid head movements by driving eye rotation in the opposite direction to generate the vestibular ocular reflex (VOR). The AOS, responding to slow velocity motion of the visual field, elicits finely graded eye movements called the optokinetic reflex (OKR) that compensate for retinal slip and stabilize slowly moving images (Masseck and Hoffmann, 2009). The AOS constitutes the primary visual system motion circuitry present in all vertebrates, including humans (Fredericks et al., 1988; Kubo et al., 2014; Masseck and Hoffmann, 2009; Simpson, 1984), and it includes subpopulations of DS ganglion cells (DSGCs) and their central targets in the midbrain. In mice, these central targets are the medial terminal nucleus (MTN) in the ventral region of midbrain adjacent to the cerebral peduncle and substantia nigra, and the dorsal terminal nucleus (DTN) and the nucleus of the optic tract (NOT), which together are located in the dorsal midbrain anterior to the superior colliculus (SC) (Dhande and Huberman, 2014).

Although AOS anatomy was described over a century ago (reviewed in Simpson, 1984), the recent development of genetic tools has aided in the identification and functional analysis of its various components (Dhande et al., 2013; Kay et al., 2011; Triplett et al., 2014; Yonehara et al., 2009; Yonehara et al., 2008). AOS brain targets receive direct retinal input from both On DSGCs and a subpopulation of On-Off DSGCs. On DSGCs, which respond to bright objects moving at slow speed, are major retinal AOS components. The dendrites of On DSGCs co-stratify with On starburst amacrine cell (On SAC) dendrites in the S4 sublamina of the retina. On DSGC axons project to all three AOS nuclei in the midbrain: the MTN, DTN, and NOT (Dhande et al., 2013; Yonehara et al., 2009; Yonehara et al., 2008). In addition to On DSGCs, a newly discovered population of On-Off DSGCs with relatively small dendritic fields and a preference for forward, slow-velocity image motion target the NOT and SC (Dhande et al., 2013). DSGC innervation of the different AOS brain targets mediates distinct OKR responses; innervation of the MTN drives vertical OKRs (vOKRs), whereas innervation of the DTN/NOT