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Spontaneous patterned retinal activity and the refinement of retinal projections

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Abstract

A characteristic feature of sensory circuits is the existence of orderly connections that represent maps of sensory space. A major research focus in developmental neurobiology is to elucidate the relative contributions of neural activity and guidance molecules in sensory map formation. Two model systems for addressing map formation are the retinotopic map formed by retinal projections to the superior colliculus (SC) (or its non-mammalian homolog, the optic tectum (OT)), and the eye-specific map formed by retinal projections to the lateral geniculate nucleus of the thalamus. In mammals, a substantial portion of retinotopic and eye-specific refinement of retinal axons occurs before vision is possible, but at a time when there is a robust, patterned spontaneous retinal activity called retinal waves. Though complete blockade of retinal activity disrupts normal map refinement, attempts at more refined perturbations, such as pharmacological and genetic manipulations that alter features of retinal waves critical for map refinement, remain controversial. Here we review: (1) the mechanisms that underlie the generation of retinal waves; (2) recent experiments that have investigated a role for guidance molecules and retinal activity in map refinement; and (3) experiments that have implicated various signaling cascades, both in retinal ganglion cells (RGCs) and their post-synaptic targets, in map refinement. It is likely that an understanding of retinal activity, guidance molecules, downstream signaling cascades, and the interactions between these biological systems will be critical to elucidating the mechanisms of sensory map formation.

Keywords: Retinal projection; Retinotopic map; Optic tectum

Contents

Abbreviations: RGC, retinal ganglion cell; dLGN, dorsal lateral geniculate nucleus of the thalamus; SC, superior colliculus; OT, optic tectum; SAC, starburst amacrine cell

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1. Introduction

The brain contains highly ordered circuitry in which sensory inputs are organized into maps that represent different features of sensory space. One dogma of developmental neurobiology is that guidance molecules mediate initial map development, while refinement of these maps requires neural activity. This underlies many hypotheses regarding the relative contribution of activity-dependent and activity-independent factors in map formation.

In the visual system, two well-studied organizational schemes are retinotopic and eye-specific maps (see Fig. 1). In this section, we introduce these maps and provide overviews of the hypotheses regarding the relative role of activity-dependent processes and guidance molecules in their development.

1.1. Overview of eye-specific and retinotopic refinement of retinal projections.

Mature retinotopic maps are organized such that a visual stimulus activates neighboring retinal neurons, which in turn project to and stimulate neighboring neurons in the corresponding target structure in the brain. For example, in the superior colliculus (SC), and its non-mammalian homolog the optic tectum (OT), the nasal–temporal (N–T) axis of the retina maps to the posterior–anterior (P–A) axis of the SC, such that stimulation of the nasal retina elicits responses in posterior SC neurons, while anterior SC neurons respond to stimulation of temporal retina. The dorsal–ventral (D–V) axis of the retina maps along the lateral–medial (L–M) axis of the SC in a similar fashion. In the dorsal lateral geniculate nucleus of the thalamus (dLGN), the N–T axis of retina maps to the D–V axis of the dLGN and the D–V axis of retina maps project to the L–M axis of the dLGN (Fig. 1).

Eye-specific maps are organized such that neurons located in distinct regions in the target structure respond to visual stimuli that activate neurons in one eye or the other. For example, axons from contralateral and ipsilateral retinas make synaptic connections with neurons in separate layers within the dorsal lateral geniculate nucleus of the thalamus, each layer receiving only ipsilateral or only contralateral input. Similarly, axons from the distinct eye-specific regions in the dLGN project to distinct alternating right-eye/left-eye columns, called ocular dominance columns, in primary visual cortex. Though the retinal projections to the SC are primarily contralateral, there is an ipsilateral projection to a distinct cellular layer in the rostral part of the nucleus (Fawcett et al., 1984; O'Leary et al., 1986; Thompson and Holt, 1989).

In mammals, the precise targeting of retinal ganglion cell (RGC) axons necessary for retinotopy and eye-specific layers emerges from initially unordered projections of RGC axons within the SC and dLGN. Within the SC, all RGC axons initially extend beyond their correct topographic position, growing toward the posterior pole (Simon and O'Leary, 1992).