Influence of spontaneous activity and visual experience on developing retinal receptive fields

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Background: The role played by early neural activity in shaping retinal functions has not yet been established. In the developing vertebrate retina, ganglion cells fire spontaneous bursts of action potentials before the onset of visual experience. This spontaneous bursting disappears shortly after birth or eye opening. In the present study, we have investigated whether the outgrowth of receptive fields in turtle retinal ganglion cells is affected by early spontaneous bursting or by early visual experience.

Results: Ganglion cells normally stop bursting spontaneously 2–4 weeks post-hatching, the time when receptive-field areas reach adult size. When turtles are reared in the dark, the spontaneous bursting persists. Concomitantly, receptive-field areas expand to more than twice those observed in normal adults. To test whether chronic blockade of spontaneous bursting inhibits the expansion of developing receptive-field areas, we have exposed the retina to curare, a nicotinic cholinergic antagonist, because spontaneous bursting by ganglion cells requires acetylcholine. Curare was released from Elvax, a slow-release polymer that was implanted in the eye. When spontaneous bursting was chronically blocked with curare in hatchlings, dark-induced expansion of receptive fields was abolished. Moreover, receptive fields of ganglion cells exposed to curare in hatchlings reared in normal light and dark cycles were smaller than normal.

Conclusions: These results strongly suggest that early, acetylcholine-dependent spontaneous bursts of activity control the outgrowth of receptive-field areas in retinal ganglion cells. The onset of visual experience induces the disappearance of the immature spontaneous bursts, resulting in the stabilization of receptive-field areas to their mature size.

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Background

Early spontaneous activity and visual experience play an important role in the development of the extra-retinal visual system [1–5]. Immature mammalian retinal ganglion cells are known to fire spontaneous bursts of action potentials [6–10]. These bursts, which are synchronized between neighboring ganglion cells [7–9], are believed to play a fundamental role in the development of connections between ganglion cells and their central targets [1–5]. Amacrine cells fire in synchrony with ganglion cells during these bursts [11–13], raising the possibility that such bursts may be involved in the development of neural circuitry within the retina itself. Although activity-dependent processes are known to affect developing dendritic structures in mammalian retinal ganglion cells [14–17], almost no information is available on possible roles of immature, sensory-independent spontaneous activity and of visual experience [18] in sculpting the functional properties of mature retinal ganglion cells.

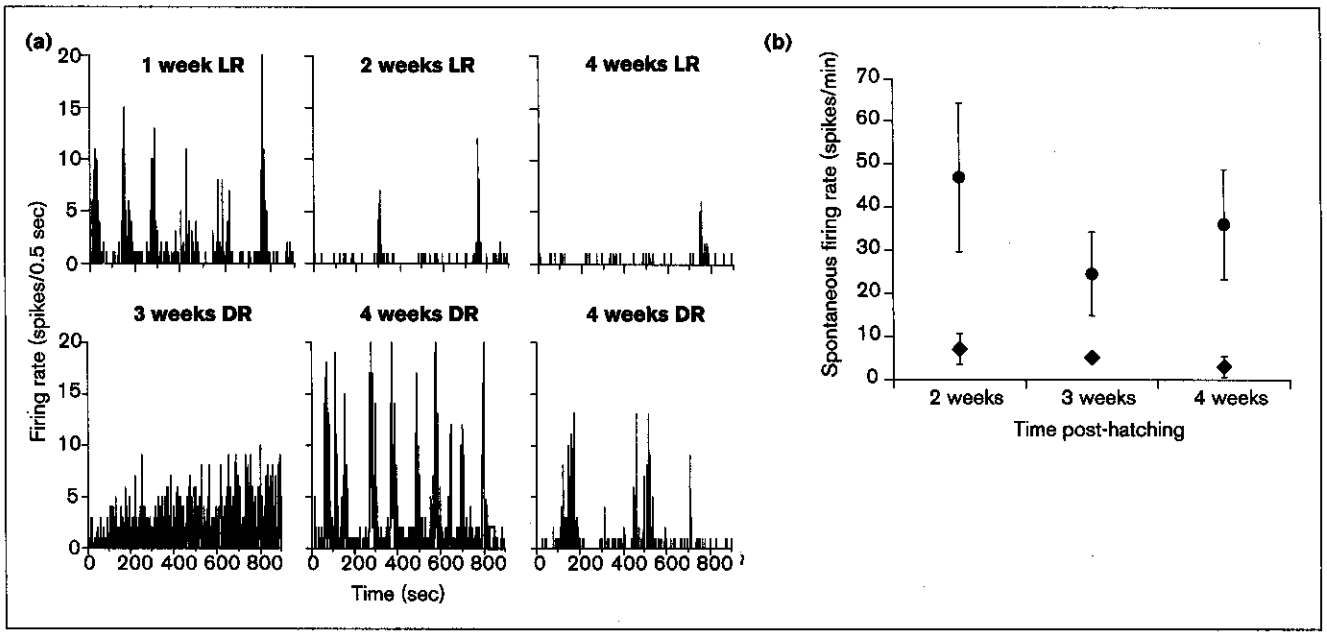
Turtle retinal ganglion cells are known to fire spontaneous bursts and to respond to light from early embryonic stages [19]. The disappearance of these bursts and the maturation of several receptive field properties coincide at 2–4 weeks post-hatching [19]. In the present study, we have investigated whether the outgrowth of receptive field areas is affected by early, sensory-independent spontaneous bursting activity and/or visual experience. We have found that the onset of visual experience induces the disappearance of the immature spontaneous bursts, and that the expansion of receptive field areas is controlled by early spontaneous bursting activity.

Results

Spontaneous bursting and visual experience

Turtle ganglion cells fire spontaneous bursts from embryonic stage 22 (~20 days before hatching or 40 days through gestation) [19]. All ganglion cells are still firing spontaneous bursts at 1 week post-hatching (Fig. 1a, upper left panel). The incidence of spontaneously bursting cells starts to decrease about 2 weeks post-hatching, and most cells become relatively quiescent by the end of the first month (Fig. 1a, upper middle and right panels). At this stage, they fire mainly isolated, sporadic spikes. Mature

Figure 1



Maintenance of spontaneous activity in ganglion cells from dark-reared turtles. **(a)** Spontaneous activity in three normal, light-reared (LR, top) and dark-reared (DR, bottom) ganglion cells during the first month post-hatching. Spontaneous activity is illustrated by changes in firing rate (in 0.5 sec bins) during recording trials of 900 sec. Burst onset and offset is indicated by abrupt changes in firing rate. The light-reared, 1 week-old ganglion cell illustrated on the far left fires strong bursts; the older cells (middle and right), fire mainly isolated, sporadic spikes. Dark-reared ganglion cells exhibit robust spontaneous firing; they fire either continuously (far left) or in bursting patterns (middle and right). **(b)** Mean spontaneous firing rate (with standard error bars) of light-reared (diamonds) and dark-reared (circles) ganglion cells sampled at 2, 3 and 4 weeks post-hatching. The pooling of ganglion cells did not distinguish between cell types, such as those at the bottom of (a). Dark-reared ganglion cells fire significantly more than light-reared ganglion cells. The number of ganglion cells at 2, 3 and 4 weeks post-hatching, respectively, were: 18, 27 and 39 (light), and 15, 18 and 20 (dark).

retinal ganglion cells in the turtle, unlike those in mammals, exhibit weak spontaneous, non-bursting activity in the dark.

When turtles are reared in the dark, however, all ganglion cells keep firing spontaneously (they were not investigated beyond the first month post-hatching) (Fig. 1a, lower panel). Although ganglion cells from light-reared turtles spontaneously fire at a low and steadily decreasing rate from 2–4 weeks post-hatching, spontaneous activity persists in ganglion cells from dark-reared turtles (Fig. 1b). Although most cells fire in bursting patterns (exemplified in the bottom middle and right panels of Fig. 1a), some cells fire rather continuously (exemplified in the bottom left panel of Fig. 1a).

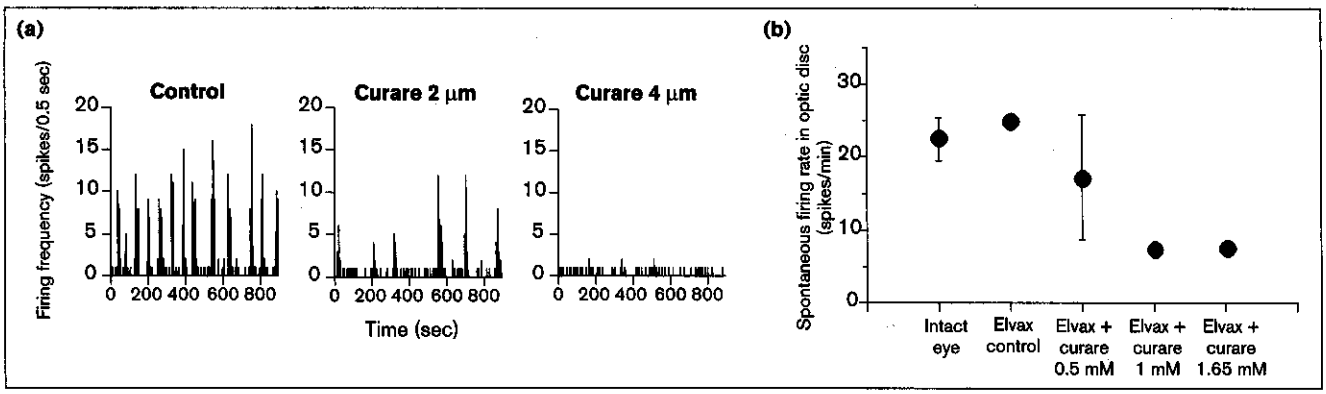
Dark-rearing and the expansion of receptive-field areas

Ganglion cells become sensitive to light soon after they start bursting spontaneously, at stage 23 (~43 days through gestation) [19]. The ganglion cell receptive-field areas expand significantly as soon as turtles hatch, and stabilize to their mature size when the spontaneous bursting stops [19]. When turtles are raised in the dark, these receptive fields become much larger than in normal hatchlings. Receptive-field areas expand significantly from the stage at which all normal ganglion cells still express robust spontaneous bursts (0.33 ± 0.04 mm^2, $n = 17$) to that at which spontaneous bursting disappears (0.44 ± 0.04 mm^2, $n = 17$). At this later stage, receptive-field areas essentially reach the adult size (0.45 ± 0.02 mm^2, $n = 20$). The receptive-field areas of ganglion cells from dark-reared turtles, however, expand already far beyond normal dimensions at 1–2 weeks post-hatching (0.73 ± 0.05 mm^2, $n = 9$), and at 4 weeks post-hatching they reach a value of 1.13 ± 0.08 mm^2 ($n = 21$). This dark-induced maintenance of spontaneous bursting and dramatic expansion of receptive-field areas, together with the coinciding maturation of receptive-field properties and disappearance of early spontaneous bursts in normal hatchlings [19], led us to hypothesize that early spontaneous activity bursting may control the outgrowth of receptive field areas.

The cholinergic nature of early spontaneous bursting

We have observed that the main excitatory synaptic drive on ganglion cells during the spontaneous bursting is mediated by acetylcholine, acting *via* nicotinic receptors [20]. Figure 2a, for example, shows how spontaneous bursts in a ganglion cell from a stage 25 (approximately the last week of gestation) embryo are blocked in a dose-dependent

Figure 2



Spontaneous bursting activity in ganglion cells is blocked by curare, a nicotinic acetylcholine receptor antagonist. **(a)** The effect of bath-applied curare on spontaneous bursting in a stage 25 embryonic ganglion cell. In the presence of 2 μM curare, both the incidence and the intensity of the bursts decreased, and they disappeared when the concentration of curare was doubled. The activity is illustrated by changes in firing rate, as in Fig. 1. **(b)** Spontaneous firing recorded from the optic disc (with standard error bars) is chronically blocked by slow curare release from the polymer Elvax 40W. The activity in ganglion cells was recorded *via* the optic disc, in whole eyes, and was thus not affected by the surrounding Ringer solution. Effective activity blockade was achieved with 1 mM curare. The eye was removed from the embryo 5–10 days following implantation. Four eyes were used for each condition.

manner by bath-application of the nicotinic antagonist curare. Similarly, curare always profoundly reduced the spontaneous firing of ganglion cells in retinae from dark-reared turtles, regardless of the initial firing pattern (some cells fire in a more burst-like pattern than others — see bottom panels of Fig. 1a). In contrast, curare does not affect the spontaneous non-burst background activity in embryos (see Fig. 2a) and normally reared post-hatching turtles. Moreover, when the spontaneous bursts disappear 2–4 weeks post-hatching in turtles reared in normal light, they are not replaced by continuous firing, which is driven by glutamate, as they are in mammals [10]. We therefore assume that the apparent continuous firing behavior of some ganglion cells from dark-reared turtles, as that illustrated in the bottom left panel of Figure 1a, reflects extremely long bursts that have merged together.

To test the hypothesis that early spontaneous bursting activity may control the outgrowth of receptive-field areas, we have used curare to block the bursts chronically. To enable constant delivery of curare to the retina, we applied the drug through the slow-release polymer Elvax 40W. Elvax 40W is an ethylene vinyl-acetate copolymer capable of sustained release of a wide variety of molecules in many different tissues *in vivo* [21], which has been shown to release drugs over a period of at least 60 days [22–24]. To test the feasibility of this technique in our preparation, we recorded spontaneous activity from ganglion cells that had been exposed to different concentrations of curare (0, 0.5, 1 and 1.65 mM) released from Elvax. The activity in ganglion cells was recorded *via* the optic disc, in whole eyes, and was thus not affected by the surrounding Ringer solution. The activity was recorded ~30 minutes after the eye had been transferred to the recording chamber.

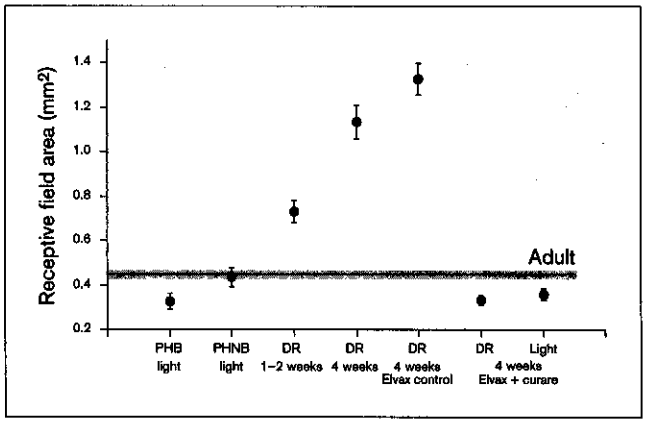
We were able to record spontaneous spikes from the optic disc of intact eyes, despite the fact that the retina was not properly oxygenated, presumably because turtles have an extremely low metabolic rate (they are capable of remaining submerged, without breathing, for at least 30 minutes). Firing recorded under these conditions was not so burst-like as in isolated retinae, but we were mainly interested in the total amount of spontaneous spikes from normal eyes, as opposed to eyes that had been exposed to Elvax–curare implants. The effect of the drug at different concentrations was measured 5–10 days following Elvax implantation, because drug release from the polymer is known to be faster during the first 24 hours and then stabilizes to a lower level [23].

Figure 2b shows how spontaneous firing recorded from the optic disc is chronically blocked by slow curare release from the polymer Elvax 40W. Effective activity blockade was achieved with 1 mM curare. There was no change in activity when retinae were exposed to drug-free Elvax. The activity decreased (insignificantly) in eyes that had been exposed to 0.5 mM Elvax–curare implants. When the curare concentration was higher, the activity dropped three-fold to a baseline level (only few isolated spikes were detected). We thus used 1 mM of curare, the lowest concentration that effectively blocks the spontaneous activity.

Early activity and the expansion of receptive field areas

To investigate how early spontaneous bursting and visual experience interact to control the outgrowth of receptive

Figure 3



The outgrowth of receptive field areas in developing ganglion cells is controlled by early acetylcholine-dependent spontaneous activity. Receptive-field areas (with standard error bars) are shown at two normal post-hatching stages (PHB, post-hatching bursting cells; PHNB, post-hatching non-bursting cells), in 1–2 and 4 week old dark-reared cells (DR), in 4 week old dark-reared cells that had been exposed to Elvax without curare, and in both dark-reared and light-reared 4 week old cells that had been exposed to 1 mM curare. Elvax blocks were implanted at hatching. Adult receptive field areas are represented by the horizontal line (with standard error as the shaded area).

field areas, curare was applied at hatching time, and turtles reared in either normal light–dark cycles or constant darkness during the first month post-hatching. Receptive-field areas of ganglion cells were then measured. Once retinae from dark-reared hatchlings chronically exposed to curare had been superfused for at least 2–3 hours in normal Ringer solution, spontaneous firing of ganglion cells occasionally resumed. This indicated that curare was still effectively blocking spontaneous firing of ganglion cells one month following implantation of the polymer, as ganglion cells from dark-reared hatchlings whose retinae had not been exposed to curare always started firing spontaneously within about half an hour of the retina being transferred to the experimental chamber.

The dramatic dark-induced expansion in receptive-field areas was completely abolished in dark-reared turtles by exposure of their retinae to curare (0.33 ± 0.02 mm^2, $n = 24$) (Fig. 3). Elvax without curare did not reduce the large receptive field areas in dark-reared turtles (1.33 ± 0.07 mm^2, $n = 13$). Exposure to light had no effect on receptive-field area outgrowth in ganglion cells from retinae exposed to curare (0.36 ± 0.03 mm^2, $n = 32$). In both dark and light rearing conditions, receptive-field areas in retinae exposed to curare were significantly smaller than in normal ganglion cells of corresponding age (1 month post-hatching). These areas were similar to those measured in immature, spontaneously bursting post-hatching ganglion cells.

Discussion

In an earlier study, we showed that embryonic ganglion cells have small excitatory receptive fields [19]. We hypothesized that such small receptive fields are due either to immature dendritic layout — of ganglion cells or presynaptic neurons such as amacrine cells — or to sparse synaptic connections between these cells. Moreover, we postulated that, when the retina matures, the receptive fields of ganglion cells expand because of dendritic outgrowth and branching [25–27], the establishment of new synaptic connections, or the reinforcement of pre-existing synaptic connections. These processes would be constantly triggered by the spontaneous embryonic bursts, the gradual disappearance of which is induced by exposure to light at hatching.

The present findings are consistent with this hypothesis. When the young retina is deprived of visual experience, ganglion cells (and perhaps amacrine cells as well) keep firing spontaneously beyond the period during which spontaneous bursts normally disappear. Consequently, our hypothesis predicts the emergence of abnormally large receptive field areas, which is exactly what we observe in our study. In addition, we find that chronic exposure to curare completely abolishes both the bursts and the dark-induced expansion of receptive field areas.

In accordance with this hypothesis, recent histological findings indicate a direct correlation between the changes we observe in expansion of receptive field areas and dendritic outgrowth. While growth cones proliferate in the inner plexiform layer in dark-rearing conditions, their number was abnormally low in retinae that had been exposed to curare (J. De Juan, N.M.G., J.V. Guardiola and E.S., unpublished data). The dendritic arbors of ganglion cells, revealed with horseradish peroxidase, are abnormally large and ramified in retinae from dark-reared hatchlings, while they are abnormally small and polarized in retinae that have been chronically exposed to curare (E.S., unpublished data).

A recent study shows that dark-rearing modifies the normal developmental course of dendritic arbors in only a specific subpopulation of retinal ganglion cells in the hamster [17]. These hamsters were reared in the dark only from post-natal days 12–22, however, so at this stage we cannot reject the possibility that prolonged dark-rearing, from birth, might have a more widespread effect on developing dendritic arbors in mammalian ganglion cells as well.

Visual experience alone — light responses do not vanish in the presence of curare — has no direct effect on the outgrowth of receptive field areas. Exposure to light, however, seems indirectly to affect developing receptive-field areas, because it induces the weakening and eventual disappearance (see Fig. 1) of the spontaneous bursts post-hatching.

The mechanisms through which visual experience may lead to the disappearance of the spontaneous bursts remain to be established.

Although mammalian ganglion cells become sensitive to light later in life than do turtle ganglion cells, it is reasonable to assume that exposure to light is involved in the disappearance of spontaneous bursts in mammals as well as reptiles. Mammalian ganglion cells start responding to light shortly after birth or eye opening, before spontaneous bursting disappears. In kittens, for instance, ganglion cells are already responsive to light by post-natal day 5, while spontaneous bursts disappear 2–3 weeks after birth [10], as in the turtle.

Our results show that early, acetylcholine-dependent, spontaneous activity plays a fundamental role in the functional development of ganglion cells. Such direct correlative studies on the role of visual experience and early spontaneous-activity-dependent mechanisms in shaping functional retinal properties have not yet been performed in mammals. However, three findings indicate that our results may be relevant to the developing mammalian retina. First, several experimental findings indicate that spontaneous bursts in immature mammalian ganglion cells are also driven by acetylcholine. Acetylcholine enhances spontaneous activity recorded in immature rabbit ganglion cells [6]. In kittens, bursts recorded from immature ganglion cells disappear during blockade of synaptic transmission, but they are not blocked by glutamatergic antagonists [10], which suggests that they might be driven by acetylcholine as well. A recent study shows that, in the immature ferret retina, waves sweeping across the ganglion cell layer, and synaptic currents recorded from ganglion cells during these waves, are also blocked by curare [28]. Second, chronic activity blockade (with tetrodotoxin and glutamatergic blockers) affects the development of dendritic structures in mammalian ganglion cells [14–16]. Finally, several major steps towards dendritic maturation in mammalian ganglion cells occur before eye opening and onset of sensitivity to light [29].

Conclusions

The results presented in this paper suggest that early neural activity, recorded from ganglion cells in the developing retina, affects the development of retinal receptive fields. Two distinct types of activity interact to shape the mature retina: first, acetylcholine-dependent spontaneous bursts of action potentials, which begin in the embryo and disappear within the first month post-hatching; and second, visual experience at hatching, for the most part not carried by acetylcholine. Our findings suggest that visual experience induces the disappearance of spontaneous bursting. The expansion of receptive-field areas of ganglion cells is directly controlled by the immature, acetylcholine-dependent activity, but not by light.

Materials and methods

The preparation

We obtained single-unit extracellular recordings of action potentials from turtle (*Pseudemys scripta elegans*) retinal ganglion cells. We recorded activity from 34 ganglion cells in seven retinae isolated from hatchlings that were dark-reared (from hatching) between 9 and 29 days; 13 ganglion cells in three dark-reared retinae that were exposed to Elvax without curare from hatching; 32 ganglion cells in six retinae that were exposed to curare from hatching; and 24 ganglion cells in four retinae that were both exposed to curare and dark-reared. The responses obtained from these cells were compared to those of normal hatchlings of similar ages and to adults [19]. All the procedures for retinal isolation, recordings, light stimulation, and data analysis were as described elsewhere [19].

Mapping of receptive-field areas

Receptive-field size was measured within 1 mm from the visual streak in adults, and in the presumed corresponding area in hatchlings [19] (no visual streak is apparent in young retinae in our preparation). To perform these measurements, we used a 9×9 array of non-overlapping squares of light. For normal retinae, and retinae that had been exposed to curare, the squares were $100 \times 100\ \mu m^2$, covering a $900 \times 900\ \mu m^2$ area on the retina. For the retinae from dark-reared turtles, where we found that receptive fields were dramatically larger, we used $166.7 \times 166.7\ \mu m^2$ squares, covering a $1500 \times 1500\ \mu m^2$ area on the retina. The squares appeared in random order and each square flickered 10 times over 12 seconds. A detailed description of receptive-field diameter calculation is given elsewhere [19]. The areas reported in this study are those of discs with the calculated diameters.

Preparation and implantation of Elvax–curare blocks

Elvax beads were washed in 100% ethanol during 3–4 days at −20 °C. For each block, five Elvax beads were dissolved in 1 ml methylene chloride. We added 10 µl of curare solution and 10 µl of 0.1% fast green in DMSO to the liquid Elvax. The Elvax–drug solutions were then frozen during 1–2 weeks to allow evaporation of the solvent. Small pieces of Elvax (~ $1.0 \times 0.5 \times 0.2$ mm) were cut for surgical implantation. Both embryos (stage 25) and hatchlings were anesthetized by hypothermia and the injection of 0.05 ml alcaïne behind the eye lid. For embryos, a window was cut in the egg shell to expose the head. Elvax was introduced in the eye through a small cut made in the sclera, near the cornea. The implanted eye (one eye per turtle) was treated during 5 days with the antibiotic gentacidin sulfate. All hatchlings and 75% of the embryos survived this surgical procedure.

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References

1. Grant S, Keating MJ: **Changing patterns of binocular visual connections in the intertectal system during development of the frog, *Xenopus laevis*. II. Abnormalities following early visual deprivation.** *Exp Brain Res* 1989, **75**:117–132.
2. Constantine-Paton M, Cline HT, Debski E: **Patterned activity, synaptic convergence, and the NMDA receptor in developing visual pathways.** *Annu Rev Neurosci* 1990, **13**:129–154.
3. Goodman CS, Shatz CJ: **Developmental mechanisms that generate precise patterns of neural connectivity.** *Cell* 1993, **72**:77–98.
4. Katz LC: **Coordinate activity in retinal and cortical development.** *Curr Opin Neurobiol* 1993, **3**:93–99.
5. Horton JC, Hocking DR: **An adult-like pattern of ocular dominance columns in striate cortex of newborn monkeys prior to visual experience.** *J Neurosci* 1996, **16**:1791–1807.

6. Masland RH: **Maturation of function in the developing rabbit retina.** *J Comp Neurol* 1977, **175**:275–286.
7. Maffei L, Galli-Resta L: **Correlation in the discharges of neighboring rat retinal ganglion cells during prenatal life.** *Proc Natl Acad Sci USA* 1990, **87**:2861–2864.
8. Meister M, Wong ROL, Baylor DA, Shatz CJ: **Synchronous bursts of action potentials in ganglion cells of the developing mammalian retina.** *Science* 1991, **252**:939–943.
9. Wong ROL, Meister M, Shatz CJ: **Transient period of correlated bursting activity during development of the mammalian retina.** *Neuron* 1993, **11**:923–938.
10. Tootle JS: **Early postnatal development of visual function in ganglion cells of the cat retina.** *J Neurophysiol* 1993, **69**:1645–1660.
11. Grzywacz NM, Sernagor E, Amthor FR: **Retinal directional selectivity: function, mechanism and development.** In *Handbook of Brain Theory and Neural Networks.* Edited by Arbib MA. Cambridge, Massachusetts: Bradford books, MIT Press; 1995:312–314.
12. Wong ROL, Chernjavsky A, Smith SJ, Shatz CJ: **Early functional neural networks in the developing retina.** *Nature* 1995, **374**:716–718.
13. Burgi PY, Grzywacz NMG: **Possible roles of spontaneous activity and dendritic growth for retinal receptive field development.** *Neural Comp* 1996, in press.
14. Wong ROL, Herrmann K, Shatz CJ: **Remodeling of retinal ganglion cell dendrites in the absence of action potential activity.** *J Neurobiol* 1991, **22**:685–697.
15. Lau KC, So KF, Tay D: **APV prevents the elimination of transient dendritic spines on a population of retinal ganglion cells.** *Brain Res* 1992, **595**:171–174.
16. Bodnarenko SR, Chalupa LM: **Stratification of ON and OFF ganglion cell dendrites depends on glutamate-mediated afferent activity in the developing retina.** *Nature* 1993, **364**:144–146.
17. Wingate RJT, Thompson ID: **Targeting and activity-related dendritic modification in mammalian retinal ganglion cells.** *J Neurosci* 1994, **14**:6621–6637.
18. Daw NW, Wyatt HJ: **Raising rabbits in a moving visual environment: an attempt to modify directional sensitivity in the retina.** *J Physiol* 1974, **240**:309–330.
19. Sernagor E, Grzywacz NM: **Emergence of complex receptive-field properties of ganglion cells in the developing turtle retina.** *J Neurophysiol* 1995, **73**:1355–1364.
20. Sernagor E, Grzywacz NM: **Synaptic connectsion involved in the spontaneous correlated bursts in the developing turtle retina.** *Inv Ophth Vis Sci* 1994, **35**:2125.
21. Silberstein GB, Daniel CW: **Elvax 40 implants: sustained, local release of bioactive molecules influencing mammary ductal development.** *Dev Biol* 1982, **93**:272–278.
22. Reh T, Constantine-Paton M: **Eye-specific segregation requires neural activity in three-eyed *Rana pipiens*.** *J Neurosci* 1985, **5**:1132–1143.
23. Cline HT, Constantine-Paton M: **NMDA receptor antagonists disrupt the retinotectal topographic map.** *Neuron* 1989, **3**:413–426.
24. Schnupp JW, King AJ, Smith AL, Thompson IA: **NMDA-receptor antagonists disrupt the formation of the auditory space map in the mammalian superior colliculus.** *J Neurosci* 1995, **15**:1516–1531.
25. Amthor FR, Takahashi ES, Oyster CW: **Morphologies of rabbit retinal ganglion cells with complex receptive fields.** *J Comp Neurol* 1989, **280**:97–121.
26. Bloomfield SA: **Orientation-sensitive amacrine and ganglion cells in the rabbit retina.** *J Neurophysiol* 1994, **71**:1672–1691.
27. Yang G, Masland RH: **Direct visualization of the dendritic and receptive fields of directionally selective retinal ganglion cells.** *Science* 1992, **258**:1949–1952.
28. Feller MB, Wellis DP, Werblin WS, Shatz CJ: **Requirement for cholinergic synaptic transmission in the propagation of spontaneous retinal waves.** *Science* 1996, **272**:1182–1187.
29. Wässle H: **Dendritic maturation of retinal ganglion cells.** *Trends Neurosci* 1988, **11**:87.