Cuddling up in the dark

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It is known that neural activity is involved in the courtship by which different nerve termi-

nals establish relations with appropriate target cells in some parts of the nervous system. But whether the relevant activity is that of the presynaptic afferent, the post-

synaptic cell or some harmony between the two has remained in question — most meth-

ods of interfering with activity perturb it on both sides. Now, on page 568 of this issue,

Hahn et al. provide compelling anatomical evidence that postsynaptic responses play a crucial role. This paper follows close behind another, in Science, that reveals greater order in the patterns of retinal activity occurring in development before vision is possible.

In mammalian and good binocular vision, the connections from the eyes to the main visual relay nucleus, the lateral genicu-

late nucleus (LGN), are arranged in layers that each receive input from one eye or the other. In a number of species, geniculate layers or sublaminae are also specific for the centre type (‘On’ or ‘Off’, responding to lightness or darkness, respectively) of the innervating retinal ganglion cell.

At the level of the single cell, the specificity of connections is even greater: about half of the geniculate cells receive their effective excitatory input from only a single retinal ganglion cell; and among cells that receive several inputs, the inputs always originate from the same eye and from retinal ganglion cells of the same centre type. Anatomical studies have revealed that single geniculate cells actually do manage this feat of ensuring that their hundreds of synaptic contacts are made with only one or a few of the hundreds of retinal afferents with which their dendritic spines overlap.

How are these synaptic partners chosen with such precision? A most attractive hypo-
thesis has been that discharge activity of reti-

nal ganglion cells is locally correlated among cells of the same centre type within each small region of the retina, so that the timing of neural activity provides a high-resolution signal of the eye of origin. Neighbourhood relationships and centre-type of each retinal terminal at every point within a target structure. If early synapses were hypo-
thesized to have the heaviest probability of them increased in strength according to the correlation between pre- and postsynaptic activity, then such input activities could lead initially diffuse projections to refine into pre-

cise maps, layers and inputs.

In normal development, retinal inputs from the two eyes initially innervate the LGN without regard to layer. Later (during the last few weeks of fetal life in the cat) they lose connections to the inappropriate regions. At the retinal level, this may be due to an ambient dark period (branching structure) in appropriate regions so as to form eye-specific layers.

Although there is no visual stimulation dur-

ing this period of life, retinal ganglion cells are active — they seem to discharge rhy-

matically, in wavelets of activity that propagate at various orientations across the retina. Blocking this pre-visual activity of the retinal nerve fibres (and probably also of the geniculate cells) by infusions of tetradotoxin into fetal brains prevents the eye-specific layers from forming.

Hahn et al. have now found that, in nor-

mal development, retinal afferent terminal arborizations are progressively confined to single geniculate sublaminae. Locally or system-

cially applying blockers of the N-methyl-D-

aspartate (NMDA) subtype of glutamate receptor, which mediates much of the input to the geniculate cells, would be expected to have little or no effect on retinal afferent activity, but it prevents the normal re-

arrangement of the arborial trees. These new results are consistent with the operation of hebbian synapses in the normal develop-

ment of retinogeniculate connections.

The NMDA receptor has attracted enormous interest, because its biophysical properties allow it to inject calcium into the postsynaptic cells specifically at synapses whose synaptic activation takes place in association with other activity that depo-

larizes the cell. In the CA1 region of the hippocampus, calcium entry through NMDA receptors seems to be necessary, and perhaps sufficient, for the long-term potent-

ation of synapses. The NMDA receptor plays a similarly crucial part in amphibian visual-system development. In the mammalian visual sys-

tem, both pre- and postsynaptic cells may be invaded anatomically and physiologically in vivo and in vitro. Future studies of this system may reveal whether calcium entry through NMDA receptors, or other some consequence of harmonic pre- and post-

synaptic activity, mediates the synaptic plasticity responsible for the development of precise synaptic connections.

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