GABA aminotransferase has been well documented (*6*). Subcellular fractions of human platelet lysates were prepared by centrifugation at 280*g* for 10 minutes and then at 10,000*g* for 30 minutes at 4°C. The aminotransferase activity of the fraction that pelleted between 280 and 10,000*g* contained 77 percent of the activity of the original platelet lysate, with a fourfold higher specific activity. Most of the remaining activity was recovered in the 280*g* pellet. Although the 10,000*g* fraction could be expected to contain platelet granules as well as mitochondria, this preliminary experiment indicates that the platelet enzyme, like brain GABA aminotransferase, may be localized in mitochondria.

Pryidoxal phosphate, the cofactor that stimulates GABA aminotransferase activity in other tissues, also stimulated the activity in human platelets. When platelet lysates were prepared in the absence of pyridoxal phosphate, the addition of 0.1 m*M* pyridoxal phosphate to assay mixtures gave a 2.7-fold increase in product formation, similar to the cofactor stimulation observed with human brain GABA aminotransferse in comparable experiments (*3*).

Another comparison between human brain and platelet enzymes was based on their susceptibility to known GABA aminotransferase inhibitors. Aminooxyacetic acid at 0.01 μM and ethanolamine *O*-sulfate at 0.3 m*M* produced partial inhibition (Table 1), and aminooxyacetic acid at 1 μM completely inhibited activity in both extracts. When rats were pretreated with these irreversible inhibitors, the platelet enzyme was strongly inhibited at doses that also affected brain GABA aminotransferase in the same animals.

Table 1 summarizes and compares properties of GABA aminotransferase from human platelets and brain. Although the enzyme activity in platelets is much lower than that in brain, other properties suggest a similarity of the enzymes in the two tissues. This is consistent with earlier studies (*3*) showing that GABA aminotransferase of human brain resembles that of liver and kidney with respect to kinetic and molecular properties and susceptibility to inhibitors. Electrofocusing experiments indicated that purified active enzyme of human brain, liver, and kidney occurs as a single molecular form (*3*).

GABA aminotransferase is analogous to monoamine oxidase (MAO) in that both are mitochondrial enzymes which mediate the catabolism of putative neurotransmitters in the CNS. Likewise, both enzymes occur in human platelets. Although platelet MAO differs in some important respects from that of brain (*7*), the feasibility of MAO assays in human blood has stimulated studies by many investigators who are searching for useful biochemical correlates between this platelet enzyme and various clinical syndromes. Similar studies may now be possible with platelet GABA aminotransferase, particularly with reference to illnesses in which aberrations in GABA metabolism have been implicated, such as schizophrenia, Huntington's chorea, epilepsy, and other convulsive disorders (*8*). Although at this time there is insufficient evidence that the activity of platelet GABA aminotransferese can be used as a measure of the brain enzyme, the potential value of such a correlation justifies further investigation.

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Development of the Rat's Uncrossed Retinotectal Pathway and Its Relation to Plasticity Studies

Abstract. *In the normal newborn rat the retinotectal pathway from each eye distributes across the whole area of both the ipsilateral and contralateral superior colliculus. Most of the ipsilateral projection retracts during the first ten postnatal days to produce the normal adult pattern, but retraction fails to occur if one eye is removed at birth.*

Each side of the vertebrate brain responds to stimulation of the contralateral visual field. In mammals, in which there is overlap of the visual fields of the two eyes, this rule is satisfied by a distribution of retinal axons at the optic chiasm such that axons originating in the retina temporal to the region which views a line directly ahead of the animal (vertical midline) generally project ipsilaterally while axons originating nasal to this region project only contralaterally. This precise segregation of fibers is achieved before the animal ever uses its visual system (*1*-*3*), but it can be substantially modified by removing one eye early in development, and variations from the normal pattern also occur in genetic mutants such as albinos (*4*). Little is known about how optic axons are directed to one or the other side of the brain during development, however, or how factors generating anomalous distributions relate to those controlling normal development.

We have investigated this problem both in normal rats and in rats with one eye removed at birth, restricting our attention to the retinal projection to the superior colliculus. There is normally only a small uncrossed retinotectal projection in the adult, but after an eye is removed at birth, this pathway enlarges to cover all areas of the superior colliculus. Whereas the normal uncrossed pathway originates from ganglion cells of the lower temporal retina, the expanded uncrossed pathway arises, in addition, from cells throughout the rest of the retina. Many of these are situated nasal to the point of representation of the vertical midline (*5*, *6*).

We examined the retinotectal projections in 28 albino and 6 pigmented rat pups ranging in age from 1 to 10 days. Fourteen of the albino animals had the left eye removed at the time of birth. The right eye of each animal was injected with 1 to 4 μl of a 30 percent solution of horseradish peroxidase (HRP) 18 to 24 hours before being killed. Animals were perfused with phosphate buffer (*p*H 7.4) containing 5 percent sucrose (weight to volume) followed by 2 percent glutaraldehyde in phosphate buffer. Frozen sections through the brains were reacted with tetramethyl benzidine (TMB) and hydrogen peroxide (*7*). The brains of

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several adult albino animals with intraocular injections of HRP were also available for comparison.

We found that the anterograde transport of HRP, coupled with the use of TMB as the chromogen, provides a more powerful tool for visualizing low-density axonal projections than other tracing methods. In part, this is because the presence of transported HRP is greatly amplified by the enzymatic reaction employed, but another advantage is the virtual absence of "background" labeling, which is a frequent problem in developmental studies using tracers such as tritiated amino acids.

In all of the animals examined, there was a dense, uniform deposition of HRP reaction product throughout the superior colliculus contralateral to the injected eye. We emphasize this fact because it suggests that the entire retina was uniformly exposed to HRP. In normal adult albino rats the uncrossed retinotectal projection seen after HRP injections is focused in the anteromedial portion of the superior colliculus (*5*), although some reaction product is present along the entire medial edge of the superior colliculus with occasional patches occurring more laterally.

The uncrossed projection in normal 1-day-old animals, however, shows a strikingly different pattern. Throughout the superficial layers of the superior colliculus there is a substantial uncrossed projection (Fig. 1A), which is denser anteriorly and medially but is still quite prominent in all other areas of the colliculus. In preliminary experiments in which we have examined the retrograde transport of HRP after small injections into one superior colliculus of newborn rats, we have consistently found labeled ganglion cells in both nasal and temporal portions of the ipsilateral retina. It seems, therefore, that all areas of the retina provide an uncrossed projection at birth, which resembles the situation we find in adult animals that were unilaterally enucleated at birth (*6*).

The uncrossed retinotectal projection in normal animals remains broadly distributed for the first few postnatal days, but by day 7 it becomes restricted to more anterior and medial portions of the colliculus. Concurrently, uncrossed fibers begin to recede from the more superficial layers (Fig. 1B). By the tenth postnatal day, the uncrossed retinotectal projection very closely resembles that of the adult (Fig. 1D). A similar series of events occurs in both albino and pigmented animals (*8*).

For the first two postnatal days, there is no detectable difference in the distribution of the uncrossed retinotectal projection of rats with one eye removed at birth compared with normal rats of the same age. By the third postnatal day there is some increase in density of the uncrossed pathway in the lateral portion of the colliculus. However, this difference may only be apparent, since the thickness of the superficial layers of the colliculus becomes severely attenuated within 2 to 3 days of enucleation. The uncrossed pathways of normal and enucleated animals are clearly distinct by 7 days. In the enucleated animals, the uncrossed retinotectal projection from the remaining eye is still prominent through-

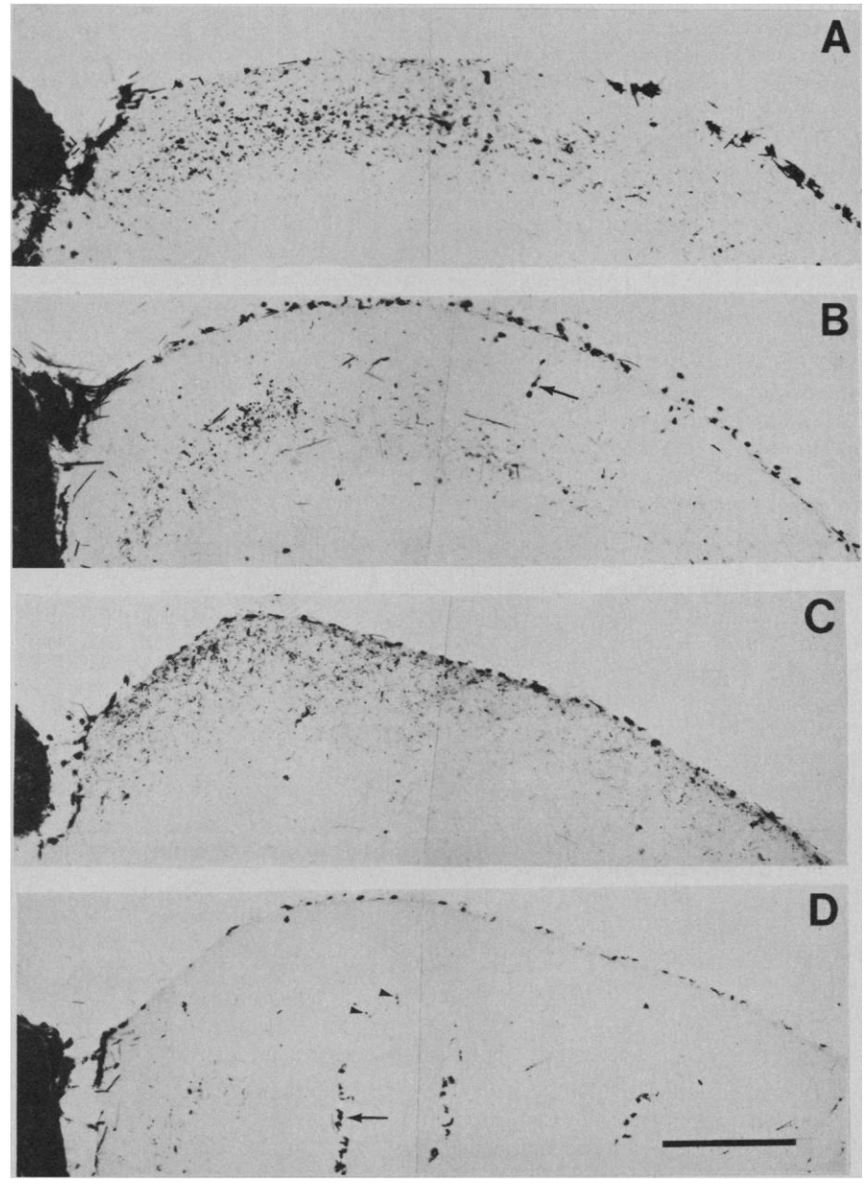

Fig. 1. Transverse sections through superior colliculi ipsilateral to intraocular HRP injections. Sections were reacted with TMB and H_2O_2 to demonstrate the presence of anterogradely transported HRP. The TMB reaction product appears as small dark granules against a light background. The dorsal surface of the colliculus is at the top of each photomicrograph. The midline and a small portion of the contralateral colliculus are to the left. Large dark granules on the surface of the colliculi and at arrows are red blood cells containing endogenous peroxidase. (A) One-day-old normal animal. An ipsilateral retinotectal projection can be seen throughout the colliculus, extending to the pial surface especially in the medial half. (B) Seven-day-old normal animal. While an ipsilateral projection can still be detected across the mediolateral extent of this section through the rostral third of the colliculus, very little reaction product is present nearer the surface. (C) Seven-day-old animal from which one eye was removed at birth. In this littermate of the animal shown in (B), an ipsilateral retinotectal projection is prominent throughout the superficial portion of the colliculus, and may be slightly denser than the ipsilateral projection at birth. (D) Ten-day-old normal animal. The ipsilateral retinotectal projection at 10 days has become restricted to a deep position in the medial portion of the colliculus, with only occasional foci (arrowheads) evident more laterally. Bar signifies 200 μm.

out all areas of the superior colliculus, although it tends to appear somewhat denser anteriorly and medially (Fig. 1C). This situation remains throughout the life of the animal (*5*).

These results show that during development a neural pathway may distribute broadly and then retract to its normal adult pattern. In the developing rat, the retinal projections from both eyes initially overlap in the superficial layers of the superior colliculus, with most of the uncrossed axons eventually retracting or dying back at least as far as the optic chiasm, if not to the retina. It remains to be seen whether the transitory uncrossed axons are branches of contralaterally directed axons, as appears to be the case in older animals (*9*).

Other studies of the developing visual system have also found an initial overlap of the inputs from the two eyes (*2, 3, 10*). In marked contrast to the present observations, however, these studies show that as development proceeds, the two inputs segregate into adjacent laminae or stripes of roughly equal size rather than one's causing the almost complete elimination of the other. This is true for the retinotectal pathway of the monkey in which the inputs from each eye spread evenly throughout the superior colliculus on fetal day 78 and then segregate into alternating stripes between days 124 and 144 (*3*). It is not clear why the retinotectal pathway of rats and monkeys should develop so differently from an initially similar pattern. The mechanisms whereby segregation or retraction of afferents occurs are not known either. Since our experiments show that removal of one eye at birth prevents the elimination of uncrossed axons, it appears that the crossed optic pathway plays a major part in this process, perhaps by competitively inhibiting the maintenance of connections of uncrossed axons.

These observations also provide a cautionary note regarding the interpretation of the results of early lesions based solely upon examination of animals at much later times. In our own earlier studies on the effects of neonatal eye removal in rats, we hypothesized that the enlarged uncrossed pathway was most likely the result of sprouting rather than, as seems to be the case, retention of an earlier developmental state (*4, 11*). It is necessary to consider the likelihood that other anomalous projections observed after early lesions also may be due to failure of retraction of a transitory pathway rather than to sprouting.

It is possible to speculate about the relation of the events observed here to the normal pattern of development of the optic chiasm. The initial distribution of axons at the optic chiasm to crossed and uncrossed sides may not be precisely controlled, although axons originating from the temporal retina may be most likely to project ipsilaterally and nasal axons may be least likely. Such a distribution could simply be a product of the mechanics of growth through the region of the chiasm. Subsequently, the retraction process, resulting from competitive interaction between uncrossed and crossed axons, may eliminate inappropriately distributed axons and lead to a precise definition of the decussation point at the chiasm. Thus the pattern of distribution of axons at the optic chiasm may not, in fact, be due to specific interactions between the axons as they grow through the chiasm; it may instead be the result of a two-part process in which there is an approximate sorting depending on mechanical factors at the chiasm and a secondary adjustment depending on competitive interactions between terminal branches of axons. The study points to a relation between early eye removal and this developmental pattern. It would be interesting to reinvestigate the anomalies found in albino animals with the current model in mind.

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Tomatine and Parasitic Wasps: Potential Incompatibility of Plant Antibiosis with Biological Control

Abstract. *α-Tomatine, an alkaloid in tomato plants, is toxic to an endoparasite of a major lepidopterous pest of tomatoes. The parasite acquires the alkaloid from its host after the host ingests the alkaloid. This form of interaction creates a potential dilemma to controlling herbivorous pests through chemical antibiosis in plants.*

Plant resistance to insects can result from the presence in various plant tissues of naturally occurring chemicals that are antagonistic or antibiotic to insect pests (*1*). Some host-plant resistance (HPR) programs are searches for selectively breeding for a high content of chemicals toxic to insects (*2*). However, little is known about the possible detrimental effects of these plant antibiotics on biological control agents (such as parasites and predators) of insect pests.

We have found that a parasite of a major agricultural pest could be poisoned by an antibiotic, α-tomatine, from tomato plants (*3*). The parasite was an ichneumonid, *Hyposoter exiguae* (Viereck), in one of its larval hosts, *Heliothis zea* (Boddie) (*4*). α-Tomatine forms a one-to-one insoluble and biologically inactive complex with many β-sterols and may induce toxic effects by impairing sterol utilization (*5*). Also, it is sapogenic and causes cytolysis (*6*). Because certain β-sterols are essential nutrients for insects (*7*), α-tomatine may be useful as an antagonist in the control of tomato pests. However, we found that the parasite *H. exiguae* can be toxified by α-tomatine, acquiring it from its less sensitive host, *H. zea*.

Our results are based on the use of artificial diets for the host containing 0.3 and 0.5 percent (wet weight) α-tomatine (*8*). Host larvae were fed on diets in five groups of 20 larvae per diet type (*9*). To

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