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PATTERNING OF CENTRAL SYNAPSES IN REGENERATION OF THE OPTIC NERVE IN TELEOSTS[1]

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IT HAD been well established by 1925 that the retina of the grafted adult urodele eye undergoes degeneration except for its ciliary portion, that a new retina is regenerated from this surviving ciliary margin, and that the new optic nerve which develops from the regenerated retina is capable of re-establishing connections with the brain (Fujita, 1913; Griffini and Marcho, 1889; Kolmer, 1923; Uhlenhuth, 1912). Whether the regenerated optic-nerve connections were capable of function, however, was still at that time a matter of controversy. Early reports, emanating from Przibram's laboratory, of visual recovery in many vertebrates, including rats, particularly the claims of Koppanyi (1923), were found to have been based on inadequate tests of vision and later came to be regarded generally as unreliable (Keeler, 1929; Stone and Zaur, 1940).

It was Matthey in 1925 and 1926 who first furnished indisputable evidence of the recovery of vision in adult urodeles after eye transplantation and also after intracranial resection of 1–2 mm. of the optic nerves. Matthey's animals would turn and swim toward a moving worm confined within a glass vessel placed within the animals' aquarium and would then try to snap at the worm through the glass. They would respond similarly toward a finger moved just above the surface of the water but not touching it. Also they would pursue and try to strike through the glass at a piece of liver moved about in the air outside the aquarium walls. These reactions were said to be entirely comparable to those of a normal animal and were absent in a blind animal. Matthey's results were later repeated and confirmed by Stone and others in this country (see Beers, 1929; Stone and Zaur, 1940).

From Matthey's description of visual

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tral-fiber tracts (Sperry, 1945*b*–48*b*), have furnished strong evidence for a general biochemical-affinity theory of the ontogenetic organization of synaptic connections. It is only in the amphibians, however, that this type of phenomenon has so far been observed. It has therefore become important to find out whether or not synaptic formation is regulated on a similar basis in other classes of vertebrates. This paper is the result of an effort to extend to teleosts the experiments on optic-nerve regeneration. Functional regeneration of the optic nerve in fishes apparently has not been reported in previous experiments, even where the nerve has been sectioned without damaging circulation (Matthews, 1933). There were encouraging indications, however, in the report of Ask and Andersson (1927) and in unpublished observations of Rasquin that the teleost optic nerve might possess some capacity for functional regeneration. The general plan of the following experiments is the same as that employed in earlier studies on eye rotation and optic-nerve regeneration in amphibians.

MATERIAL AND METHODS

The fishes used were of various species as designated below and were collected in March around the island of Bimini in the West Indies. They were maintained in the laboratory in groups of approximately ten in aquaria 60×30×30 cm. with running sea water at 24°–29° C. and were fed every other day. The animals were anesthetized in a solution of 1.2 per cent urethane in sea water and were then wrapped in damp cleansing tissue and operated upon out of water with the aid of a dissecting microscope. The only other instruments used were fine scissors and watchmaker's forceps.

In order to rotate the eyes, all the extrinsic ocular muscles were extirpated either through a dorsal incision into the orbit in *Bathygobius soporator* (Cuvier and Valenciennes) and *Canthigaster rostratus* (Bloch) or through a complete circular incision around the conjunctiva in all other species. The eyeball, thus freed except for the intact optic nerve and associated blood vessels, was then rotated through 180° on the optic axis and allowed to set a few moments before the fish were returned to water. Only one eye was rotated. The contralateral optic nerve was sectioned, and a segment of it was excised to prevent its regeneration. When it became evident that further precaution in this regard was necessary, the unrotated eye was completely excised in all the *B. soporator*, and the optic nerve in the other species was again severed and partially excised 3 weeks after the initial operation.

The optic nerve was sectioned through a short dorsal incision in the conjunctiva. The eyeball was rolled downward to make the optic nerve accessible from the dorsal approach. The nerve was pinched repeatedly with forceps until complete division of the nerve substance was visible. In many cases the outer sheath of the nerve, which is tougher than the nerve proper, was left partially intact to help guide the regenerating fibers. When optic-nerve division was performed in conjunction with eyeball rotation, the rotation was always carried out prior to nerve division.

The types of reactions used in estimating the quality of visual performance and recovery included (*a*) the optokinetic responses induced by rotation of a striped drum around the animals in the horizontal plane; (*b*) the spontaneous optokinetic reactions which have been found to follow eye rotation (Sperry, 1943*a*); (*c*) avoidance of obstacles, such as the aquarium fixtures, large shells, and other fish, while swimming at high speed; (*d*) recovery it could be inferred not only that the regenerating fibers were successful in establishing functional connections in the brain but, furthermore, that the central relations were formed with a sufficient degree of orderliness to permit discrete perception and accurate localization of small objects in space. This was particularly remarkable because nerve regeneration under such conditions is attended by extreme distortion of the normal intraneural fiber pattern. Matthey himself observed that the regenerating fibers failed to restore the orderly fascicular pattern of normal ontogeny and that there was a tendency for some of the optic fibers to become entangled in neuromas and for other stray fascicles to become lost in atypical pathways.

That the recovered vision had, nevertheless, been adaptive, despite the observed disorder among the regenerated fibers would suggest either that (*a*) the fibers had managed to untangle and sort out in an extraordinary manner after reaching the brain centers or else that (*b*) some functional process of adaptation, like learning or conditioning, was instrumental in the adjustment of the central connections. The latter possibility seemed to be favored by the inclusion among Matthey's animals of two cases in which, after resection of the optic chiasma, the regenerating nerves had connected atypically with the ipsilateral, instead of the contralateral, brain center and also by the inclusion among the recoveries described by Stone and his students of cases in which the eyeball had been rotated through 90° and 180°. Presumably, it could be only by means of some process akin to learning that normal vision could be recovered in the face of anatomical rearrangements of this kind.

More detailed analysis of the functional aspects of this problem, however, has since revealed (Sperry 1942–44) that rotation of the eye causes definite and marked symptoms of inverted vision and that, in contradiction to the above, the same type of abnormal vision is restored after optic-nerve regeneration with the eye rotated. It has likewise been found that, when the regenerating optic nerves are intentionally made to connect to the ipsilateral optic centers, the recovered visual responses are clearly misdirected to the contralateral side (Sperry, 1945*a*). Apparently, the earlier failures of Matthey, Stone, and others to observe these functional abnormalities may be attributed to the fact that they did not include optokinetic reactions among their tests of recovery and that they were not considering the neurological problems involved and therefore overlooked the misdirection of localizing responses that were present in their animals.

Further investigation of the functional aspects of optic-nerve regeneration in conjunction with eye rotation, contralateral transplantation of eyes, cross-union of optic nerves, and optic-lobe lesions in urodeles and also in larval and adult anurans of a number of different species (Sperry, 1942–45*a*) has made it clear that the organizational forces involved in the adjustment of the central synaptic associations are quite independent of functional adaptation. Apparently, the developing retinal field undergoes a polarized differentiation, as a result of which the ganglion cells of different retinal loci and the optic fibers arising from them become biochemically specified. The formation of central synapses would seem to be regulated by selective affinities between the different types of optic fibers and the various kinds of central neurons.

The results of optic-nerve regeneration, reinforced later by similar findings in regeneration of other nerves and cenescape reactions involving flight away from approaching objects, usually a small net with a frame 10×12 cm., and location of shelter; and, lastly, (*e*) positive localizing reactions, such as the seizing of small particles of food floating in the water or sinking to the bottom and the pursuit of other fish. The extent to which any one of these different reactions could be used to test vision varied considerably in different species. By employing the entire battery of tests, however, it was possible to obtain criteria of visual performance in all species which were adequate for the purposes of the experiments. In general, the optokinetic response was found to be less satisfactory than in amphibians and accordingly was relied upon to a lesser degree.

In some of the animals, rotation of the eye was attended by loss of vision, due probably to the cutting-off of circulation or to compression of the twisted optic nerve. These animals were discarded from the experiments, as were also some others that became infected and some that expired before vision was recovered after nerve division. Losses from such causes were negligible among *B. soporator*, a hardy tide-pool form, but were approximately 50 per cent among the other species.

The animals with regenerated nerves were subsequently prepared for microscopic examination by the Bodian silver proteinate method.

RESULTS

180° ROTATION OF THE EYE

The right eye was successfully rotated without loss of vision, and the left optic nerve was excised in eight *B. soporator*, two *Sparisoma radians* (Cuvier and Valenciennes), two *Abudefduf saxatilis* (Linnaeus), two *Pomacentrus leucostictus* (Müller and Troschel), and one *C. rostratus*. These fishes ranged between 4 and 10 cm. in length. In general, their subsequent behavior indicated that the reorientation of the retina had caused an illusory 180° rotation in the appearance of the visual field. The evidence of this optic inversion varied somewhat in detail in the different species.

The most striking effect of the shift in retinal orientation was the forced circling activity which it caused. The *P. leucostictus* turned continuously thereafter around a fixed spot close to the bottom of the aquarium, as a result of which they fanned out deep excavations in the sand in which they continued to rotate incessantly day after day. Their circling ceased only at night and for brief moments when they bumped against the aquarium walls, fixtures, or other fish. Food impaled on a fine wire was presented from the blind side in a position such that they turned directly into it. Under these conditions food was regularly taken after the first week with little interruption of the circling activity.

The *A. saxatilis* also circled continuously, but not in a fixed spot like the *P. leucostictus*. They swam in circles of a diameter approximately five times their total length at varying depths, keeping away from the bottom and walls of the aquarium. The *S. radians* rested most of the time on the bottom under the shelter of seaweed; but, whenever these fish were aroused from the bottom, they whirled wildly at very high speed in circles of a diameter roughly that of their total length. The circling movements of *B. soporator* were usually restricted to turning the head with the body held in place by the modified ventral fins by which these fish cling to the bottom and even to vertical glass walls. Not infrequently, however, they darted and twisted spasmodically in complete circles, sometimes at high speed. Occasionally, backward swimming, tilting, side-slipping, and various peculiar gyrations were also exhibited in the various species, indicating illusory movement of the visual field in other planes.

Optokinetic responses induced by a revolving drum were made in the direction opposite from normal by all species. Unlike the amphibians, the fish, in most cases, responded to movement of the visual field in either direction, even though one eye was blind. The spontaneous circling reactions described above were also made in both directions except in the *P. leucostictus*, which always circled toward the blind side. The responses tended to be stronger and more frequent toward the blind side, but one *A. saxatilis* circled continuously toward the seeing side. Getting started toward one side or the other seemed to reinforce further turning toward the same side.

Both the imposed and the spontaneous optokinetic reactions were accompanied by nystagmic movements of the left blind eye, the extrinsic muscles of which had been left intact. The slow phase of the movements corresponded in direction with that of the body movement. Nystagmus was extremely marked in *S. radians*, slight in *B. soporator*, and of intermediate degrees in the other species and was correlated, apparently, with the relative amount of compensatory eye movement to which they are inherently subject under normal conditions. The nystagmus frequently continued independently when head and body movements were inhibited and when the fish were resting on the bottom. These independent eye reactions were particularly pronounced in *S. radians*.

Directional reversal of responses toward and away from objects were obscured in part by the persistent forced circling. The *S. radians*, for example, circled so rapidly whenever they stirred that any localizing reactions were impossible. Erroneous localization was evident, however, in some of the other species. The *A. saxatilis*, *C. rostratus*, and *P. leucostictus* circled upward when a small net approached them from above and downward when it approached from below. The *B. soporator* darted forward when the net approached from in front, and they turned back toward the net when it approached from the rear. Often the fishes swam directly into the net under these conditions. Conversely, the *A. saxatilis* and the *P. leucostictus*, after they had become accustomed to the feeding procedure, circled upward when food was presented below them and downward when it was offered above. The *B. soporator* started forward when the lure was offered to the rear, turned backward when it was presented in front, and occasionally snapped downward when it was presented close above them.

One of the *P. leucostictus* assumed an inverted color phase characteristic of this species at night or after it has been blinded by optic-nerve section. All the *B. soporator* became extremely dark, in marked contrast to the light color of control and unoperated cases. Two extra cases with both eyes rotated also became very dark. Brief attempts to demonstrate adaptation to overhead lighting instead of to the bottom were unsuccessful, and the consistent change to the dark-color phase following eye rotation in this species remained unexplained. It has been observed that the color changes of these fishes are considerably influenced by factors other than that of the background (Beebe, 1931).

Mock operations were performed on a series of control cases, including two *B. soporator*, two *A. saxatilis*, and two *P. leucostictus*. The operations were similar in every way to those performed on the experimental group, except that the eye was left in its normal orientation. The mock operations, however, failed to produce any of the symptoms of reversed vision which followed rotation of the retinal field in the experimental group.

Effect of experience.—The cornea of the *C. rostratus* became increasingly cloudy and opaque, beginning on the 2d day after operation. By the 6th day after operation this animal was no longer circling or showing other signs of vision, and it died 3 days later. All the other cases survived the first 14 days after operation with the eye in good condition. There was little or no evidence of any re-education at this time. The free-swimming species circled a trifle more slowly than during the first 2 days, and the circling seemed to be done with less intensity and in a more automatic and relaxed fashion. When excited, however, they circled as rapidly as at the beginning, and they still exhibited directional reversal of responses to food objects and a small net.

One *S. radians* was found dead on the 15th postoperative day, without having shown any signs of readjustment. During the next 3 days the two *A. saxatilis* became weaker and expired, apparently from insufficient food intake plus the excess activity involved in their continuous circling. There were some signs of adaptation in the latter two cases, in that other responses could be superimposed upon the forced circling movements to a greater degree and more effectively than at the beginning. They continued to show directional reversal, however, in their attempts to escape a net or to approach food particles. The second *S. radians* survived 22 days. During the last 6 days it had ceased to swim in circles. Its swimming at this time was erratic and unsteady, and efforts to avoid an approaching net remained inefficient. Locomotion was greatly improved, however, over that of the first 2 weeks, when the rapid forced circling had predominated. The unrotated blind eye continued to exhibit nystagmus.

At 24 days after operation the two *P. leucostictus* were still turning continuously in circles, but the diameter of the circles had increased approximately four times and the fishes swam at slower speed. Other reactions concerned with feeding and avoidance of obstacles were superimposed, to a greater extent than at the beginning, upon the circling reactions. When excited, however, the fishes both relapsed into their earlier rapid and intense circling behavior. One of the cases was found dead on the 25th day. The other continued to improve by swimming in circles of ever increasing diameter until it was traveling in ovals as large as the aquarium would permit. By the 32d day after operation it was able to swim straight forward most of the time. The final observations on this case were made on the 45th day after operation. At this time the fish ordinarily swam straight, but, when excited by the introduction of a stick or a net into the aquarium, it reverted to its typical forced circling activity. Its optokinetic reactions in the rotating drum were still made in the direction opposite from normal. Localizing responses to food objects and an approaching net, likewise, were still definitely in reverse. All the eight *B. soporator* survived in good condition for the full 45 days. No signs of any corrective re-education were noted in this species.

The present experiments were not designed to determine whether fishes can eventually adapt themselves to inversion of the retinal field. The tests were not administered frequently enough to serve as a basis for training, nor was any special effort made to train the fishes (for example, to avoid an approaching net). The results suggest, however, that adaptation is possible to some extent in certain species. The forced circling was corrected by two animals. Although no evidence of correction of the directional reversal of localizing responses was detected, certainly the possibilities of such adjustment with further training appeared to be much more promising in these fishes than in the amphibians.

The observations were carried far enough to determine the outstanding features of inverted vision, to show that it is highly maladaptive and that it is corrigible, if at all, only after a considerable period of time. The results demonstrate satisfactorily for the purposes of the experiment that eye rotation can be employed in fishes as an adequate means for determining whether learning or related types of functional adaptation play an essential role in the recovery of vision following optic-nerve regeneration.

SECTION OF THE OPTIC NERVE

Both optic nerves were transected by the method described above in nine *B. soporator*, eight *Thalassoma bifasciatum* (Bloch), five *Halichoeres bivittatus* (Bloch), four *A. saxatilis*, and one *A. analagous* (Gill). The fishes of this group ranged from approximately 2 to 8 cm. in length. In colliding with the aquarium walls and other objects, in failure to locate food quickly or to startle at sudden movements of objects around the aquarium or to escape a small net, and in various additional species-specific activities, the behavior of all cases was indicative of total blindness.

Restoration of vision tended to occur sooner in the smaller fishes. Startle responses and optokinetic reactions reappeared as early as the 6th and 7th days after operation in the smallest *B. soporator* and *H. bivittata*, respectively. By the 14th day after operation, the majority of fishes had recovered vision in at least one eye. By the 20th day all had recovered except the *A. analagous*. The latter began to show signs of recovery on the 26th day after operation and appeared to be well recovered on the 38th day. Two additional *A. analagous* had died on the 16th and 19th days, respectively, without having shown any signs of recovery.

After optic-nerve regeneration, visuomotor co-ordination appeared to be entirely normal in quality in all cases. The fishes turned in the correct direction in making the optokinetic reactions and in the escape and feeding responses. They were able to locate and swim directly to small particles of food sinking in the aquarium or lying on the bottom, to pursue efficiently other fish, to dart into small distant crevices when startled, and to avoid the aquarium fixtures and other obstacles when swimming at high speed. As far as the tests could determine, their behavior was indistinguishable from that of normal fish. No attempt was made to measure visual acuity, and this quantitative aspect of vision may well have been subnormal, owing to loss of fibers in the scar region and the failure of others to establish functional relations in the centers. The tests were sufficient, however, to show clearly that the re-establishment of functional relations between retinal field and brain centers had taken place in an orderly, discriminative manner. Systematic selectivity of some kind was clearly present in the recovery process.

OPTIC-NERVE SECTION WITH EYE ROTATION

Eye rotation was combined with severance of the optic nerve to find out whether the orderliness of functional recovery observed to follow optic-nerve regeneration in the preceding group was dependent upon any type of functional adaptation, such as learning or conditioning. If under these conditions the fishes recovered vision which was systematically reversed like that produced by rotation of the eye with optic nerve intact, the orderliness of recovery must be ascribed to organizational factors operating in the regeneration process itself, independent of functional adaptation. In fourteen *B. soporator,* ranging in length from 21 to 63 mm., the eye on one side was rotated on its optic axis through 180°, and its optic nerve was severed. Twelve days after the primary operation the contralateral eye was excised.

On the 12th postoperative day, six of the fourteen cases already exhibited definite forced circling reactions following removal of the unrotated eye. By the 17th postoperative day, all fourteen cases were displaying the typical forced circling reactions indicative of reversed vision. When tested on the 18th day, all exhibited optokinetic responses in the direction opposite from normal. Elicitation of reversed localization and escape responses similar to those observed after simple eye rotation left no further doubt that the functional relationships between retina and brain had been restored in the same systematic manner in this group as in the preceding group. The fact that the recovery of function in this group was maladaptive, owing to the rotation of the eyes, ruled out functional adaptation as a possible factor responsible for the orderly adjustment of central synapses.

The fishes were all in the light-color phase when the unrotated eye was excised, including those that had already recovered vision. Consistent with the results of eye rotation with nerve intact, they all changed during the next several days into the dark phase, in which they remained until the termination of the experiments.

At the time of sacrifice, 41 days after the initial operation, these *B. soporator* were still exhibiting spontaneous circling reactions, reversed optokinetic reactions, and reversal of the localizing responses involved in feeding and flight.

HISTOLOGICAL CHECKS

Microscopic examination of the regenerated optic nerves following silver impregnation revealed that the nerve fibers had undergone copious regeneration from the peripheral stump and had re-established a large optic-nerve connection from the retina to the brain at the optic chiasma. The regenerated fibers were easily traced from the chiasma along their normal course into the contralateral optic lobe. In most cases the size of the optic nerve was not noticeably reduced beyond the point where it had been sectioned. Throughout the scar region the fibers were profusely interwoven with one another in fascicles of varying size (see Fig. 1). It was obvious that the orderliness of functional recovery had not been due to an indifferent mechanical guidance of fibers across the lesion into their original specific channels.

DISCUSSION

With respect to the manner in which the optic fibers re-established their central associations in the brain, the present findings are essentially the same as those obtained earlier in amphibians (Sperry, 1942–44). Previous discussions are thus applicable in large measure to the present results and need not be repeated. Despite haphazard intermixing of fibers in the scar region, the formation of synaptic relations took place in a systematic, strictly predetermined manner, with no regard for functional adaptiveness. The results indicate that the optic fibers in teleosts, as in amphibians, are qualitatively specified through embryonic differentiation of the retinal field and that this specification determines the types of synaptic associations formed in the centers. The re-

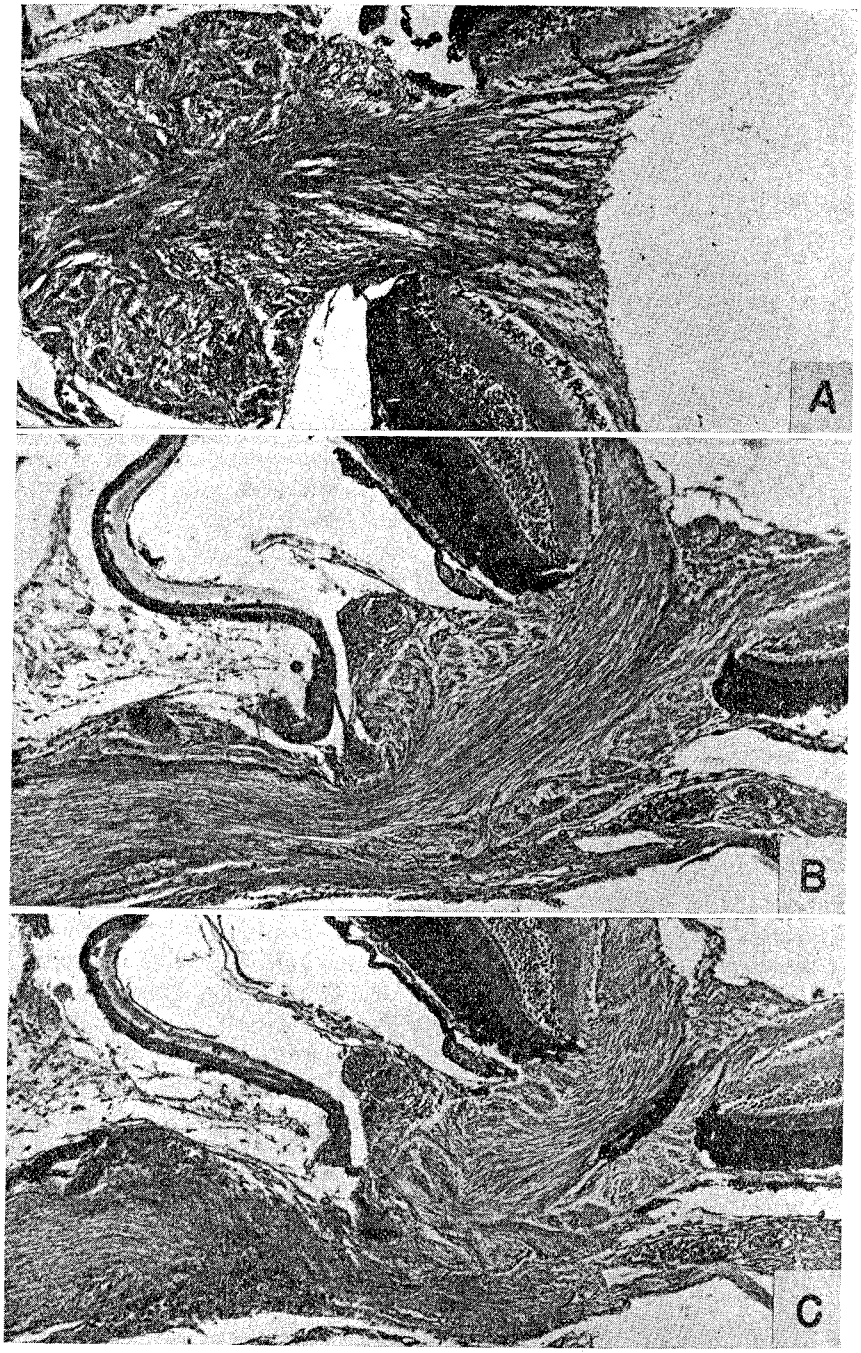

FIG. 1.—Photomicrographs of 10-μ sections of regenerated optic nerves of *B. soporator*. Optic fibers emerging from eyeball toward right run a tangled, tortuous course through the neuromatous scar before entering cental nerve stump at left. In *B* fibers running through central core of scar take a relatively direct route, but in *A* the fiber pattern, even in center of scar, is disorganized. *B* and *C* are from the same nerve, with *B* nearer center of scar. $\times$150.

Despite this extreme disorientation of the regenerating optic fibers, the re-establishment of functional relations in the brain was orderly and systematic.

sults strengthen the supposition that the principles of synaptic formation derived from the amphibian studies are not peculiar to the class Amphibia but apply also to the nervous system of other vertebrates.

Visual recovery following optic-nerve division was slightly quicker in some of these fish than even the most rapid recovery obtained previously under similar conditions in amphibians (Sperry, 1944). Both function and histological appearance also indicated that regeneration in general was fully as good or better in the fishes. Failure of the optic nerve to reestablish central connections under similar conditions in *Fundulus heteroclitus* (Matthews, 1933) remains unexplained.

Correlated with their more highly developed optic brain centers, certain of the fishes showed greater promise than had any amphibians of being able to achieve some motor adaptation to the inversion of the retinal field. The beginnings of certain minor adjustments appeared in three free-swimming species. Two cases succeeded within the brief time-span of the experiments in correcting the forced circling reactions except under conditions of unusual excitement. Whether this represented an act of learning or of some other form of functional adaptation cannot be said without further analysis. The reversed localization of objects remained uncorrected in these cases. In contrast to the foregoing free-swimming species, the *B. soporator*, which cling to the bottom most of the time, failed to show any signs of re-education, although all eight of these animals survived in good condition for the entire observation period of 45 days.

SUMMARY

1. Rotation of the eyeball on its optic axis through 180° (with optic nerve and major blood vessels remaining intact) in fifteen fishes, including six species from four different families, produced in all cases definite symptoms of inverted vision, such as forced circling, reversed optokinetic reactions, and misdirected localizing responses. For the most part these reactions remained uncorrected within the 45-day observation period. The forced circling, however, after the first 2 weeks, began to be inhibited in varying degree in several of the free-swimming species.

2. Both optic nerves were divided, producing total blindness in twenty-seven fishes, including five species from three different families. All cases exhibited a rapid and excellent recovery of visuomotor reactions, which in character were indistinguishable from normal.

3. Optic-nerve division was combined with eye rotation on one side in fourteen *B. soporator*. The contralateral eye was excised. All cases recovered the systematically inverted type of visuomotor reactions such as result from eye rotation with the optic-nerve connections left intact.

LITERATURE CITED

Ask, F., and Andersson, E. 1927. Zur Frage der Replantationsmöglichkeiten des Vertebratenauges im Lichte einiger neuerer Untersuchungen. Acta ophth., 4:97–163.

Beebe, W. 1931. Notes on the gill-finned goby. Zoologica, 12:55–66.

Beers, D. 1929. Return of vision and other observations in transplanted amphibian eyes. Proc. Soc. Exper. Biol. and Med., 26:477–79.

Fujita, H. 1913. Regenerationsprozess der Netzhaut des Tritons und des Frosches. Arch. f. vergl. Ophth., 3:356–68.

Griffini, L., and Marcho, G. 1889. Sur la régénération totale de la rétine chez les tritons. Arch. ital. biol., 12:82–89.

Keeler, C. 1929. The functional capacity of transplanted adult frog eyes. Jour. Exper. Zool., 54:461–72.

KOLMER, W. 1923. Die Replantation von Augen. V. Histologische Untersuchungen an transplantierten. Augen. Arch. f. Entw'mech. d. Org., **99**: 64–75.

KOPPANYI, T. 1923. Die Replantation von Augen. II. Haltbarkheit und Functionsprüfung bei verschiedenen Wirbeltierklassen. Arch. f. Entw'-mech. d. Org., **99**:15–42.

MATTHEWS, S. 1933. Changes in the retina of *Fundulus* after cutting the optic nerve and the blood vessels running to the eye. Jour. Exper. Zoöl., **66**:175–92.

MATTHEY, R. 1925. Récupération de la vue après résection des nerfs optiques, chez le *Triton*. Compt. rend. Soc. biol., **93**:904–6.

———. 1926. Récupération de la vue après greffe de l'œil chez le *Triton* adulte. *Ibid.*, **94**:4–5.

———. 1926. La Greffe de l'œil. Étude expérimentale de la greffe de l'œil. chez le *Triton* (*Triton cristatus*). Arch. f. Entw'mech. d. Org., **109**:326–41.

———. 1926. La Greffe de l'œil. I. Étude histologique sur la greffe de l'œil chez la larve de *Salamandre* (*Salamandre maculosa*). Rev. suisse zool., **33**:317–34.

SPERRY, R. 1942. Reestablishment of visuomotor coordination by optic nerve regeneration. Anat. Rec., **84**:470.

———. 1943*a*. Effect of 180 degree rotation of the retinal field on visuomotor coordination. Jour. Exper. Zoöl., **92**:263–79.

———. 1943*b*. Visuomotor coordination in the newt (*Triturus viridescens*) after regeneration of the optic nerve. Jour. Comp. Neurol., **79**:33–55.

———. 1944. Optic nerve regeneration with return of vision in anurans. Jour. Neurophysiol., **7**: 57–69.

———. 1945*a*. Restoration of vision after cross-union of optic nerves and after contralateral transplantation of eye. *Ibid.*, **8**:15–28.

———. 1945*b*. Centripetal regeneration of the 8th cranial nerve root with systematic restoration of vestibular reflexes. Amer. Jour. Physiol., **144**:735–41.

———. 1947. Nature of functional recovery following regeneration of the oculomotor nerve in amphibians. Anat. Rec., **97**:293–316.

———. 1948*a*. Mechanisms of neural maturation. In: Handbook of experimental psychology, ed. S. S. STEVENS. New York: John Wiley & Sons (in press).

———. 1948*b*. Orderly patterning of synaptic associations in regeneration of intracentral fiber tracts mediating visuomotor coordination. Anat. Rec., **102**:1–13.

STONE, L., and ZAUR, I. 1940. Reimplantation and transplantation of adult eyes in the salamander (*Triturus viridescens*) with return of vision. Jour. Exper. Zoöl., **85**:243–69.

UHLENHUTH. 1912. Die Transplantation des Amphibienauges. Arch. f. Entw'mech. d. Org., **33**: 723–47.