Efferent Fibers in the Visual System of the Mouse

By

Ryohei Honjin, Kyoichi Hiramatsu, Hikaru Taniguchi and Akira Nakamura

Department of Anatomy, School of Medicine, University of Kanazawa, Kanazawa
(Director: Prof. Dr. Ryohei Honjin)

Anatomical evidence of the presence of efferent fibers in the visual systems of vertebrates is fragmentary and to a large extent controversial. The efferent nerve supply to the sensory receptors including the visual system, however, is important in the physiology of regulation of the sensitivity of the receptors. The presence of efferent fibers in the retina was first suggested by Ramón y Cajal (1889). Since then, anatomical and physiological investigations of the efferent fibers in the visual system have been attempted from several different standpoints by many researchers. Among them, Armstrong (1951) discovered undegenerating fibers in the optic nerve of the snake after sectioning of the optic nerve. He construed these fibers to be efferent in character. This observation was confirmed in the human optic nerve by Wolter and Liss (1956) and Wolter (1956) and in toads by Maturana (1958). On the other hand, Bodian (1937) and Packer (1941) working with marsupials and Hess (1958) with fetal guinea pigs failed to discover any persisting optic nerve fibers after removal of the eyes. Such being the case, it is clear that this problem must be studied in many animal species for elucidation of the true state of affairs. The purpose of this study was to ascertain the existence of efferent fibers in the visual system of adult mice, utilizing the degeneration of afferent fibers in the optic system following removal of the eyeball.

Materials and Methods

Male mice (KH-A strain of Mus wagneri var. albula) were used in this study. Besides observations of normal animals, observations
were also made of animals subjected to one of two types of degeneration experiment: (1) enucleation of one eyeball; (2) enucleation of both eyeballs. After removal of the eyes, the injured animals were allowed to survive for different lengths of time. Then the entire brain with the optic nerves, in every case, was exposed rapidly and placed in fixing fluid. For the fixing and staining of both normal and degenerated nerve axons, a modified photographic silver method was employed (Honjin, 1951). The brain of 3 normal mice were cut into transverse, horizontal and sagittal serial sections 12 μ thick. The brains of 20 mice in which the right eyeball had been enucleated were also cut into serial sections. Of these, 10 were cut transversely and the other 10 horizontally, all at 12 μ. Postoperative survival times for this group of animals were 2, 3, 4, 5, 7, 9, 11, 13, 50 and 125 days. The brains of 2 mice in which both eyeballs had been enucleated were cut horizontally into serial sections. The survival times for this group were 10 and 45 days following the operation.

Results

Axonal Degeneration

Two days after the operation, the severed nerve fibers in the central stump of the optic nerve do not indicate the occurrence of any remarkable changes. They show only a slightly increased affinity for silver as compared with unsevered fibers. After 3 days, masses of fusiform swelling began to appear along the fibers like beads and in some places the slender segments between swellings show signs of rupture. This tendency becomes more marked 4 days after the operation when the severed nerve axons begin to disintegrate and are altered into fragmental rows and granular masses. By 5 and 7 days, the axonal disintegration is more advanced and coarse fragments are present throughout the primary visual pathway. The fragments disappear after 9 days, leaving only a small amount of argentophil debris (Fig. 1). The 13th day series show a similar pattern but with more advanced stages of resoluption (Figs. 2, 3, 4). The granular debris gradually loses its affinity for silver. Traces of granular debris are still present after 13 days, but none at all can be seen in the 50th and 125th postoperative days (Fig. 5). During the occurrence of these above mentioned changes in the axons, the glial cells show proliferative changes. As a consequence, in the later stage of degeneration, the primary visual pathway as-
sumes a glial strand stained pale-brown, in which a few normal appearing nerve fibers remain unchanged. The distribution of these fibers in the brain will be described later.

Unilateral Enucleation of an Eyeball

After enucleation of the right eyeball, almost all of the nerve fibers in the right optic nerve undergo degeneration. However, a few of them remain unchanged (Fig. 1). The degenerated fibers in the optic nerve of the operated side can be followed to the optic tract of the contralateral side across the optic chiasma. They correspond to the afferent fibers which originate in the ganglion cell layer of the retina of the right eye. The degenerated fibers in the left optic tract can be followed by massive axonal fragments toward the first optic center. They run through the center following the usual course of the optic tract and form a well marked layer, lying for the most part over the outer surface of the lateral geniculate body. Many of the degenerated fibers in the optic tract can be traced into the lateral geniculate body, while some of them proceed around the lateral geniculate body to the superior colliculus. Degenerated fibers which enter the pulvinar thalami are obscure. After enucleation of the right eye, no degenerated fibers can be found in the left optic nerve nor the right optic tract.

During the early stages of axonal degeneration as well as after resoluition of axonal debris, a few nerve fibers of normal appearance are still present in the central stump of the homolateral optic nerve as was mentioned above (Fig. 1). These persisting fibers are scattered throughout the nerve, but are slightly more numerous medially than elsewhere. These fibers vary in size; some of them are fine and others are thick (Fig. 1). They can be traced from the optic nerve of the homolateral side to the opposite optic tract across the optic chiasma and furthermore, from there toward their center in the brain along the pale-stained and degenerated optic tract (Fig. 2). Investigation indicates that some of the persisting fibers in the optic nerve of the operated side issue from the lateral geniculate body of the contralateral side and others of them originate from the superior colliculus of the contralateral side (Figs. 3, 4, 5). Beyond these points it was impossible to distinguish the original cells of these persisting fibers in the centers since the nerve cell bodies and their processes near the cell body were stained poorly by the impregnation method used in this study.
Enucleation of both Eyeballs

In the course of the study, the questions arose whether some of the persisting fibers found in the opposite optic tract after the unilateral removal of an eye were not uncrossed afferent fibers with their origin in the retina of the opposite eye passing through its optic nerve to enter the same optic tract without crossing in the chiasma, and moreover, whether some of the persisting fibers in the optic nerve in the homolateral side were not derived from the homolateral efferent centers. In consequence then, an experiment of enucleation of both eyeballs was attempted.

After removal of both eyeballs, many nerve fibers in the optic nerves and optic tracts of both sides undergo degeneration. However, a few fibers of normal appearance are still present in both optic nerves and optic tracts (Figs. 6, 7, 8). It is relatively easy to trace the course of the persisting fibers in this experiment, since the persisting fibers are far fewer than the degenerating ones and they can be traced clearly and distinctly in the pale-stained primary visual pathway after removal of both eyes. It is evident that the persisting fibers cross completely in the optic chiasma. This indicates that the misgivings mentioned above are groundless.

Discussion

After the first demonstration of centrifugal fibers in the retina by Ramón y Cajal (1889, 1894, 1911), the presence of these fibers was again noted by Dogiel (1895), Polyak (1941) and Wolter (1957). Physiological evidence for the presence of efferent fibers in the optic system was provided by Arey (1916) who showed the influence of one section of the optic nerve on the pigment cells of the retina in fish. Granit (1955) demonstrated changes in the sensitivity of the retina after stimulation of the mid-brain tegmentum of the cat. He concluded that this response was due to excitation of a centrifugal pathway to the retina. Död t (1955) found on recording from the retina of the rabbit that stimulation of the optic tract gave rise to a short latency antidromic spike and a second spike of appreciably longer latency which he regarded as evidence for centrifugal conduction.

Pérlia (1889) observed that the nucleus isthmo-opticus (his "nucleus opticus medialis") was completely atrophied in a chicken in which an eye had been removed shortly after birth. This result
was confirmed by Huber and Crosby (1929). More direct anatomical evidence was demonstrated by the discovery of degeneration in the optic tract of birds by Wallenberg (1898). He made lesions in the nucleus isthmo-opticus (his 'ganglion isthmi') and traced the resulting degeneration by the Marchi method through the isthmo-optic tract to what he considered to be its termination in the ganglion cell layer of the retina. This observation was confirmed by Kosaka and Hiraiwa (1915), and recently the experiment was more thoroughly replicated by Cowan, Adamson and Powell (1961) and Cowan and Powell (1962, 1963) using both the Nissl and Nauta methods. However, these reports are limited to observations of birds only, and apparently none of mammals.

Present observation clearly demonstrates that efferent nerve fibers are present in the visual system of the mouse. They were present in every animal examined (more than 20). They can be recognized in the visual pathway of the mouse even 125 days after enucleation of the eye (Fig. 5). It is difficult to believe that it is possible for a nerve axon severed from its cell body to remain undegenerated for several months. Evidence has been presented here for the presence of efferent fibers not only in the optic nerve, for they are also identifiable in the optic chiasma and optic tract. In the present experiment, the efferent fibers can be followed through this whole course. They originate partly in the lateral geniculate body and partly in the superior colliculus and run along the periphery of the optic tract. There is no clear evidence concerning the exact origin of the efferent fibers in the optic system of mammals, though Perlia (1889), Wallenberg (1898), Kosaka and Hiraiwa (1915), Huber and Crosby (1929) and Cowan and Powell (1962, 1963) provided evidence for the efferent character of the tractus isthmo-opticus in birds. Armstrong (1951), in the snake, and Maturana (1958), in the toad, respectively observed that efferent fibers are crossed in the optic chiasma. However, the present observation of mice indicates that all the efferent fibers cross completely in the optic chiasma in a like manner to the afferent fibers of the optic system of this species of animal. There is no evidence of a centrifugal projection to the homolateral eye. In any case, a comprehensive investigation of this problem in many species of animals will be necessary in the future for elucidation of visual functions.
Summary

The brains with the optic nerves of 25 mice were impregnated with silver at intervals up to 125 days following either unilateral or bilateral enucleation of the eyeballs for investigation of efferent fibers in the optic system. Serial sections were examined in every case for axonal degeneration in the optic pathway. Results obtained were as follows:

1. The optic nerve of the mouse consists mainly of fibers of retinal origin, but also contains a small number of efferent fibers.
2. All the retinal fibers completely decussate in the optic chiasma; there are no uncrossed retinal fibers.
3. The efferent fibers originate partly in the superior colliculus and partly in the lateral geniculate body.
4. The efferent fibers completely cross at the optic chiasma and run to the retina of the opposite eye passing through the optic nerve. There are no uncrossed efferent fibers in the mouse optic system.

Literature Cited

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### Explanation of Plate

Fig. 1. Longitudinal section of the right optic nerve 9 days after enucleation of the right eyeball. The fragmentary debris of axonal degeneration has almost disappeared. Note the efferent nerve fibers which remain unchanged in the altered optic nerve stained pale-brown. ×690.

Fig. 2. Longitudinal section of the left optic tract 13 days after enucleation of the right eyeball. Several efferent nerve fibers which remain unchanged can be seen. ×150.

Fig. 3. Longitudinal section of the left optic tract 13 days after enucleation of the right eyeball. Note the efferent nerve fiber which issues from the lateral geniculate body (arrow). The other persisting efferent fibers in the optic tract come from the superior colliculus of the mid-brain. ×100.

Fig. 4. Longitudinal section of the left optic tract 13 days after enucleation of the right eyeball. This micrograph was taken of a more proximal part of the left optic tract than that of Fig. 3. Many persisting efferent fibers which issue from the superior colliculus and run along the periphery of the altered optic tract are seen. ×150.

Fig. 5. Longitudinal section of the left optic tract 125 days after enucleation of the right eyeball. Note the fine and thick efferent fibers which remain unchanged in the optic tract. ×690.

Fig. 6. Longitudinal section of the right optic tract 10 days after enucleation of both eyeballs. Note that a few efferent fibers remain unchanged. ×300.

Fig. 7. Longitudinal section of the left optic tract 10 days after enucleation of both eyeballs. Note the efferent fibers which remain unchanged. ×300.

Fig. 8. Longitudinal section of the left optic tract 10 days after enucleation of both eyeballs. All the afferent fibers have undergone degeneration and disappeared. A few efferent fibers remain unchanged in the altered optic tract. ×300.
Plate

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