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REPORT DOCUMENTATION PAGE

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1. REPORT NUMBER SAM TR # 81-358		2. GOVT ACCESSION NO. AD A132 231	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) HISTOPATHOLOGY OF EXPERIMENTAL OPTIC TRACT HEMIANOPIA		5. TYPE OF REPORT & PERIOD COVERED	
7. AUTHOR(s) Robert E. Schmidt, Colonel, USAF, BSC Thomas J. Tredici, Colonel, USAF, MC Patrick S. O'Connor, Lieutenant Colonel, USAF, MC		6. PERFORMING ORG. REPORT NUMBER 81-358	
1. PERFORMING ORGANIZATION NAME AND ADDRESS USAF School of Aerospace Medicine (VSP) Aerospace Medical Division (AFSC) Brooks Air Force Base, Texas 78235		8. CONTRACT OR GRANT NUMBER(s)	
11. CONTROLLING OFFICE NAME AND ADDRESS USAF School of Aerospace Medicine (NG) Aerospace Medical Division (AFSC) Brooks Air Force Base, Texas 78235		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS 62202F 7755-17-17	
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office)		12. REPORT DATE	
		13. NUMBER OF PAGES	
		15. SECURITY CLASS. (of this report) Unclassified	
		15a. DECLASSIFICATION/DOWNGRADING SCHEDULE	
16. DISTRIBUTION STATEMENT (of this Report) Approved for public release; distribution unlimited.			
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)			
18. SUPPLEMENTARY NOTES			
19. KEY WORDS (Continue on reverse side if necessary and identify by block number) Hemianopia Optic tract resection Optic nerve degeneration Retinal ganglion cell degeneration			
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Optic nerve and retinal degeneration were studied histopathologically following surgical resection of the right optic tract of a rhesus monkey (<i>Macaca mulatta</i>). Seven months following resection, well-developed patterns of degeneration were seen bilaterally in optic nerves and retinas. The lesions correlated well with clinical studies done on the animal and with lesions reported in one case in man. The experimental results indicate that the rhesus monkey would make a good model to study optic nerve and retinal degeneration.			

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Ophthalmic Research

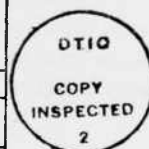
Managing Editor: O. Hockwin, Bonn

SeparatumPublisher: S. Karger AG, Basel
Printed in Switzerland

Ophthalmic Res. 14: 354-360 (1982)

**Histopathology of Experimental Optic Tract
Hemianopia¹***Robert E. Schmidt^a, Thomas J. Tredici^b, Patrick S. O'Connor^b*^aVeterinary Sciences Division, and ^bClinical Sciences Division, USAF School of
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Key Words. Hemianopia · Optic tract resection · Optic nerve degeneration · Retinal ganglion cell degeneration

Abstract. Optic nerve and retinal degeneration were studied histopathologically following surgical resection of the right optic tract of a rhesus monkey (*Macaca mulatta*). 7 months following resection, well-developed patterns of degeneration were seen bilaterally in optic nerves and retinas. The lesions correlated well with clinical studies done on the animal, and with lesions reported in 1 case in man. The experimental results indicate that the rhesus monkey would make a good model to study optic nerve and retinal degeneration.

Recent papers [Bell and Thompson, 1978; O'Connor et al., 1982; Savino et al., 1978] have presented the clinical findings associated with spontaneous optic tract lesions in man and experimental tract lesions in rhesus (*Macaca mulatta*) monkeys. However, there are few morphologic studies of the neuroophthalmic structures associated with either acquired or experimental tract lesions.

Unsold and Hoyt [1980] described the histologic pattern of band atrophy of the left optic nerve in a 45-year-old woman with a giant supraclinoid right carotid aneurysm. Leinfelder [1940] studied the retinas and optic nerves of cat and monkeys following resection of the optic nerve, and reported that the amount of degeneration in the optic nerves of the monkeys was insignificant compared to that seen in their optic tracts. He also said that there was no obvious retinal ganglion cell loss. Retinal ganglion cell loss has been reported following lesions of the optic chiasm

¹ Poster presentation at the American Academy of Ophthalmology Annual Meeting, Atlanta, November 1-6, 1981.

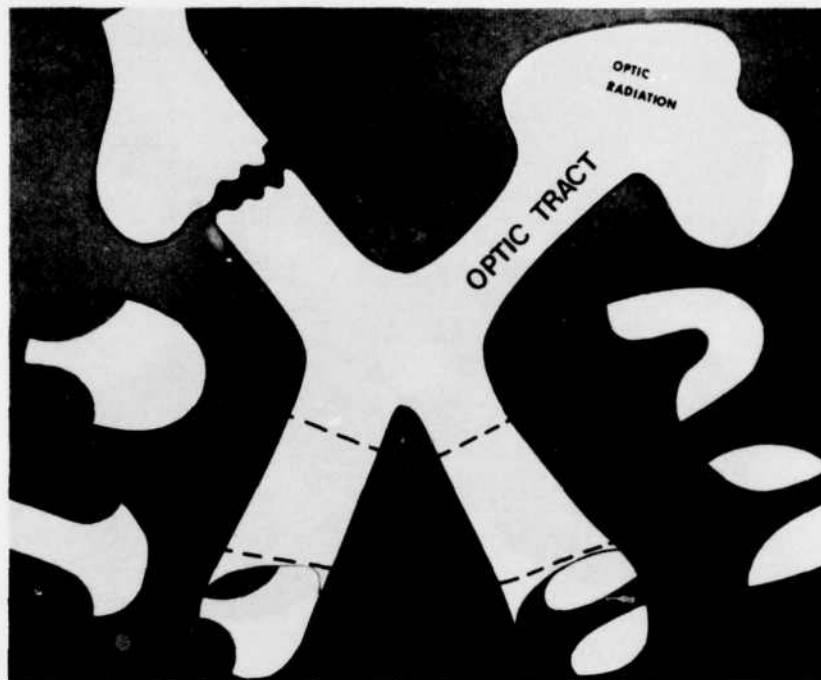


Fig.1. Diagrammatic representation of surgical site and areas of optic nerve sectioned for histology. The dark areas are zones of nerve degeneration.

of man [Kupfer, 1963]. Descending optic nerve degeneration and loss of ganglion cells has been experimentally produced in the squirrel monkey [Quigley et al., 1977] following optic nerve section.

This study was done to document and correlate the morphologic changes in the retinas, optic nerves, optic chiasms, optic tracts and brain following unilateral surgical resection of an optic tract in rhesus monkeys.

Materials and Methods

Animal Statement: The animals involved in this study were procured, maintained, and used in accordance with the Animal Welfare Act of 1970 and the 'Guide for the Care and Use of Laboratory Animals' prepared by the Institute of Laboratory Animal Resources - National Research Council.

The surgical procedures and clinical measurements of pupillary responses have been previously described [O'Connor et al., 1982]. 7 months following surgery the animal was



Fig. 2. Absence of right optic tract (arrow).

anesthetized with Nembutal and killed by perfusion with 2,500 ml 5% dextrose followed by 3,000 ml of cold Karnovsky's fixative. The eyes, optic nerves and brain were removed in toto and areas of interest photographed. The optic nerves were marked dorsally with India ink, and 4.0-mm sections from proximal, middle and distal portions of the nerve were cut (fig. 1) and embedded in paraffin by standard methods. Sections of retina, optic chiasm, optic tract and brain were also embedded in paraffin. A second set of optic nerve and retinal sections were processed and embedded in epon. All paraffin-embedded material was cut at 6 μ m and stained with hematoxylin and eosin and Luxol fast blue. Epon-embedded material was cut at 1 μ m and stained with toluidine blue.

Results

Gross Description

The right temporal muscle was pale and appeared to be approximately half normal size. A portion of the right temporal bone was gone. The right optic tract was almost entirely ablated (fig. 2).

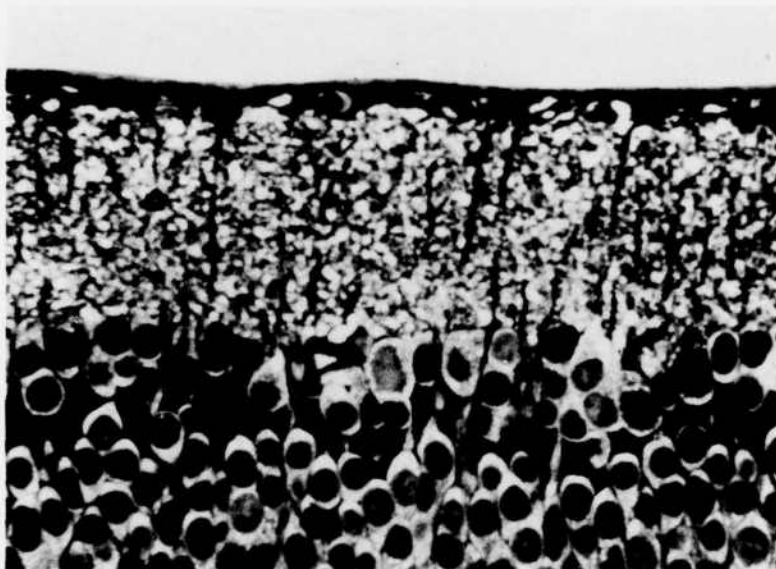


Fig.3. Retina of left eye. Note loss of nerve fiber layer and atrophic ganglion cells Toluidine blue. $\times 650$.

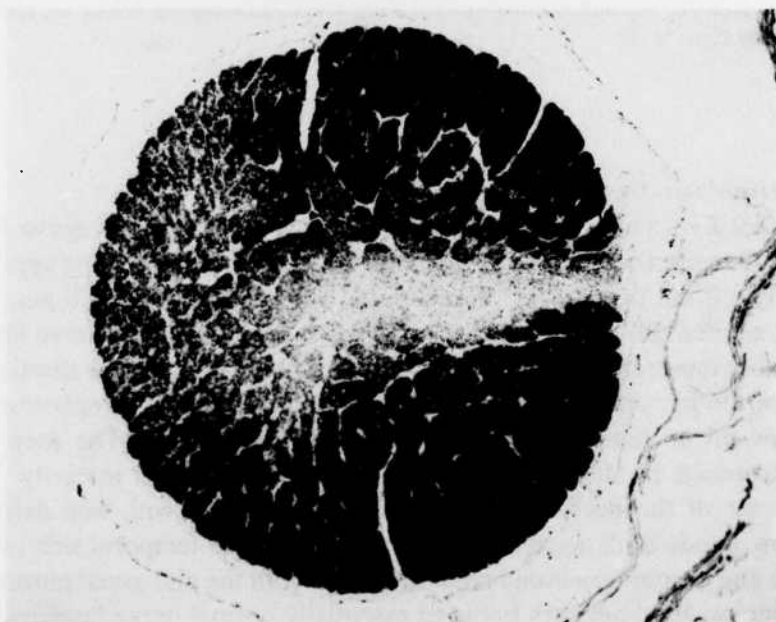


Fig.4. Mid-zone of left optic nerve. An area of degeneration extends from a narrow temporal band to a broad area nasally. Luxol fast blue. $\times 33$.

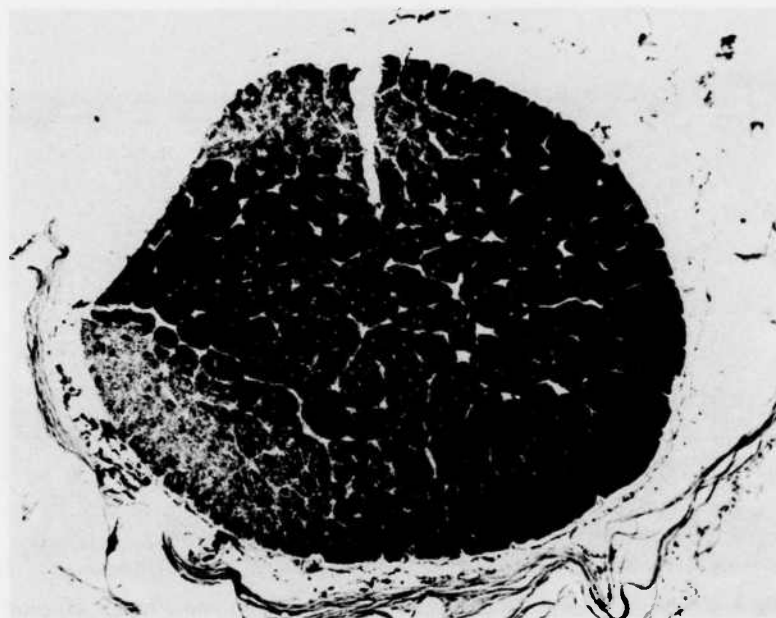


Fig. 5. Two areas of degeneration on the temporal side of the distal right optic nerve. The cut area dorsally and the diagonal cut along the dorsal-temporal border are artifacts. Luxol fast blue. $\times 29$.

Histologic Description

Left Eye. There was almost total absence of the retinal nerve fiber layer. Ganglion cells were shrunken, with those remaining being approximately $8.0\ \mu\text{m}$ in diameter as compared with a normal of $23.0\ \mu\text{m}$. The dark, condensed band in the area of what should have been nerve fibers, probably represents remaining Mueller cell fibers (fig. 3). The distal portion of the left optic nerve had a well-demarcated band of degeneration, narrow on its temporal side with a broad flare nasally. The area was characterized by demyelination and loss of architectural integrity. The mid-zone of the nerve was similar to the distal area with well-defined, narrow bands of demyelination extending from the temporal side of the nerve and becoming a broad nasal area (fig. 4). In the mid-zonal portion of the nerves, the boundary between essentially normal nerve fascicles and severe demyelination was distinct. Other areas of partial destruction of fascicles were adjacent to areas of almost total loss of myelin and apparent

hypercellularity. The proximal portion of the left optic nerve had a similar contrasting pattern of myelination and demyelination, however, on the temporal side of the nerve, the degeneration did not extend to the edge of the nerve. Severe demyelination was noted in the optic chiasm, especially the right side, however, bands of severe degeneration extended across approximately three-fourths of the chiasm with only the far left portion being free of severe degeneration.

Right Eye. The retina of the right eye was histologically similar to that of the left. The distal portion of the right optic nerve had two well-defined areas of degeneration and myelin loss. These were primarily on the temporal side of the nerve and extending dorsally and ventrally, respectively (fig. 5). The normal areas of nerve had a wide nasal expansion and a more narrow extension between the areas of degeneration. The mid-zone of the right optic nerve had a pattern of degeneration similar to that of the distal portion. The proximal portion of the nerve was similar to that of the mid-zone and distal portions.

Discussion

Although other studies [Leinfelder, 1940] of monkey retina and optic nerve following section of optic tracts have been done, little optic nerve or retinal damage was reported as much as 60 days following resection. The type of monkey used in the study was not mentioned, and some species difference may account for this lack of lesions.

Other studies [Anderson, 1973; Quigley et al., 1977] indicated that descending degeneration seemed to involve entire primate optic nerve axons at once, and that in the first 6 weeks following optic nerve transection axons were affected along their whole length abruptly, and as early as 3 weeks following resection. These studies suggested that distance from injury site to nerve cell bodies is not the most important factor in the timing of degeneration, and loss of retinal ganglion cells was independent of distance of the cell body from the injury site.

Our results correlate well with the morphologic lesions seen in a human case [Unsold and Hoyt, 1980] and with the clinical findings [O'Connor et al., 1982] indicating that the pattern of fibers in the optic nerves and tracts is similar in man and the rhesus monkey. This similarity makes the rhesus a good experimental model for research into conditions involving retina, optic nerves and optic tracts.

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Received: January 15, 1982; accepted: May 25, 1982

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