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AN ANALYSIS OF CEREBRAL CONTROL OF REFLEX PUPILLARY DILATATION IN THE CAT*

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ABSTRACT

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OBJECT

The objects of this project were to determine (1) whether the sympathetic and/or parasympathetic systems are active in controlling reflex pupillary dilatation following cerebral excitation, (2) the course which the reflex pathways follow, and (3) the degree of activity of the pupillary light reflex during stimulation of cerebral pupillodilator areas.

RESULTS

In fourteen experiments following excitation of the gyri proeus, genualis and subcallosus, a bilateral 2-5 mm. reflex pupillary dilatation occurred due to inhibition of parasympathetic activity. Hypothalamic stimulation caused a 6-8 mm. reflex mydriasis due to sympathetic activity. Evidence suggests that the reflex fibers originating in the gyri proeus, genualis and subcallosus pass through the hypothalamus to the Edinger-Westphal nucleus.

The light reflex was abolished during the excitation of the cerebral pupillodilator areas but reappeared following the disappearance of the pupillary dilatation.

CONCLUSIONS

1. Cerebral reflex pupillary dilatation in cats follows adequate excitation of the gyri proeus, genualis and subcallosus.

2. Cerebral reflex pupillary dilatation is due to active inhibition of parasympathetic activity. No sympathetic component was demonstrated.

3. Evidence suggests that centrifugal frontal lobe fibers controlling reflex pupillary dilatation by active inhibition of parasympathetic activity pass through the hypothalamus to the Edinger-Westphal nucleus.

4. The light reflex is abolished during excitation of the cerebral reflex pupillodilator areas.

RECOMMENDATIONS

None.

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AN ANALYSIS OF CEREBRAL CONTROL OF REFLEX PUPILLARY DILATATION IN THE CAT

I. INTRODUCTION

Pupillary dilatation in animals following cerebral electrical stimulation has been reported by several early workers (1,2,3,4,11,15). In 1900, Sherrington's work on dogs demonstrated that pupillary dilatation following cerebral excitation was due to inhibition of parasympathetic activity (16). Succeeding work on cats and dogs has substantiated his observations (5,6,13,17,18). However, Karplus and Kreidl reported the existence of a sympathetic subcortical pupillodilator center in the cat's tuber cinereum under control of the orbital gyrus (10).

The purpose of this project was to determine (1) whether the sympathetic and/or parasympathetic systems are active in controlling reflex pupillary dilatation following cerebral excitation, (2) the course which the reflex pathways follow, and (3) the degree of activity of the pupillary light reflex during stimulation of cerebral pupillodilator areas.

The pathogenesis of anisocoria following cerebral trauma is controversial. Hutchinson was the first to describe the dilated, fixed pupil resulting from oculomotor nerve impingement in patients (7,8). The majority of cases with anisocoria have since been explained by this mechanism (9,12,14). However, it has recently been shown that in two thirds of a large series of head trauma cases the ipsilateral dilated pupil reacted well to light, subsequent autopsy examinations revealed no oculomotor nerve impingement, and other observations suggested a cerebral control of pupillary activity (20). Since the majority of the above cases had associated cerebral hematomas, additional experiments are in progress in which the effects of such experimentally induced lesions in animals are being studied in relation to the correlation of cerebral and oculomotor nerve compression with the degree of anisocoria and light reflex activity. It is hoped that such work, together with the present communication, will lay the ground work, for clarification of the mechanism producing ipsilateral pupillary dilatation in the presence of a normal light reflex.

II. EXPERIMENTAL

A. Apparatus and Methods

1. Sacrifice experiments were performed on fourteen cats. Each animal was anesthetized with sodium pentobarbital injected intraperitoneally in amounts ranging between 35-45 mgm./kilo. The right cerebrum was exposed and the head fixed to a Horsley-Clarke apparatus modified to the extent that the instrument was bolted to the table and could be adjusted in the longitudinal axis of the table by means of an eccentric cam (see Figures 1 and 2). From this apparatus a bipolar concentric needle electrode delivered one-second bursts of sixty cycle current at 3-6 volts at millimeter intervals throughout the anterior three-quarters of the right cerebrum. The pupillary responses were observed through a lens at a magnification of two times and recorded as mild (2-3 mm.), moderate (3-5 mm.), and marked

(5-8 mm.). The course of each experiment extended over a 14-16 hour period. The brains were perfused in vivo with 10 per cent formalin U.S.P., and preserved for a week. The brains were then embedded in paraffin and serial coronal sections made at 10 mμ thickness. Every tenth section was stained by the Weil technique. The anatomical structures involved were projected on millimeter paper, identified and correlated with pupillary responses.

2. To determine which portion of the autonomic nervous system participated in cerebral control of reflex pupillary dilatation, selective nerve sections were made. Right superior cervical sympathectomies were made on two cats, followed by a thorough cerebral exploration. Removal of sympathetic activity permitted observations to be made on the intact and sympathectomized pupil following excitation of the frontal lobe. One cat, in addition to a right cervical sympathectomy, had a right ciliary ganglionectomy. The denervated pupil's function was compared to that of the intact pupil following routine stimulation. In addition, the sympathectomized pupil was compared with the intact pupil during stimulation of the hypothalamus which is the origin of sympathetic activity.

3. The course which the reflex fibers follow was demonstrated upon hypothalamic excitation in preparations with right superior cervical sympathectomies.

4. Light reflex activity was tested by shining 100 foot-candles of light into the left pupil simultaneously with each cerebral stimulus.

B. Results

1. Stimulation of Pupilloexcitatory Areas

The results of a representative experiment shown in Figure 3 demonstrate the location of the cerebral pupilloexcitatory areas. In all experiments the responsive areas were limited to the gyri proeus, genualis and subcallosus. When excited, a mild to moderate bilateral dilatation occurred. The duration of a typical response is seen in Figure 4 (dotted line curve); the extent of dilatation is shown in Figure 5. The result of hypothalamic stimulation was a marked bilateral mydriasis accompanied by activity of the nictitating membrane, piloerection, and baring of the foreclaws. In the latter, the latent period was not discernible (see Figure 4, broken line curve).

2. Nerve Section

Selective nerve sections were made to demonstrate whether cerebral excitation activated the pupil reflexly through the sympathetic or parasympathetic system.

Right superior cervical sympathectomies were made on two cats. The subsequent excitation of the gyri proeus, genualis and subcallosus still caused a normal pupillary response as shown in the dotted line curve in Figure 4. However, in the same preparation following hypothalamic stimulation, in addition to the overt sympathetic response mentioned above, the sympathectomized pupil followed the course shown by the broken line in

Figure 4. Subsequent intravenous injection of 0.5 cc. of 1:000 adrenalin caused bilateral maximal pupillary dilatation for three minutes followed by slow contraction. This showed that the pupils were still functional.

A right superior cervical sympathectomy and ciliary ganglionectomy were performed on one cat. The denervated pupil assumed the constricted size seen in Figure 6, and remained so throughout the following fourteen hours in spite of the stimulation of the cerebral reflex pupillo-excitatory areas. The left pupil reacted normally as seen in Figure 5. Again intravenous injection of 0.5 cc. of 1:1000 adrenalin caused a prolonged bilateral mydriasis similar to that in the sympathectomized preparations.

3. The Light Reflex

The light reflex was always abolished during the excitation of the cerebral pupillodilator areas. The reflex reappeared immediately following the disappearance of the pupillary dilatation.

III. DISCUSSION

The experiments substantiate the existence of cerebral reflex pupillodilator areas which function by inhibition of parasympathetic activity as shown by Magown et al. (6). They also show that the excitatory areas are restricted to the gyri proeus, genualis and subcallosus. These areas lie first superior and anteromedially and then descend caudally to the hypothalamus (see Figure 3). The subsequent passage of these reflex fibers through the hypothalamus was demonstrated in preparations with a right superior cervical sympathectomy. Following hypothalamic stimulation the sympathectomized pupil dilated slowly to 4 mm. (see dotted line in Figure 4), whereas the intact left pupil responded by rapid maximal dilatation accompanied by other overt sympathetic activity (see broken line in Figure 4). The sympathectomized pupillary reaction demonstrating the existence of projections from the gyri proeus and genualis in the hypothalamus is present but hidden by the more dominant sympathetic pupillary dilatation in preparations with bilaterally intact pupils.

The pupillodilator control over the tuber cinereum reported by Karplus and Kreidl to lie in the orbital gyrus could not be demonstrated. However, Ward and Reed reported areas 8 to contain a sympathetic pupillodilator center in monkeys (19). It is possible that the cerebral sympathetic control over the pupil becomes dominant as the animal scale is ascended.

The consistent abolition of the light reflex is to be expected during excitation of cerebral pupillodilator areas with subsequent inhibition of the Edinger-Westphal nucleus since the origin of the efferent arc of the light reflex pathway is located in this nucleus.

IV. CONCLUSIONS

1. Cerebral reflex pupillary dilatation in cats follows adequate excitation of the gyri proeus, genualis and subcallosus.

2. Cerebral reflex pupillary dilatation is due to active inhibition of parasympathetic activity. No sympathetic component was demonstrated.

3. Evidence indicates that centrifugal frontal lobe fibers controlling reflex pupillary dilatation by active inhibition of parasympathetic activity pass through the hypothalamus to the Edinger-Westphal nucleus.

4. The light reflex is abolished during excitation of the cerebral reflex pupillodilator areas.

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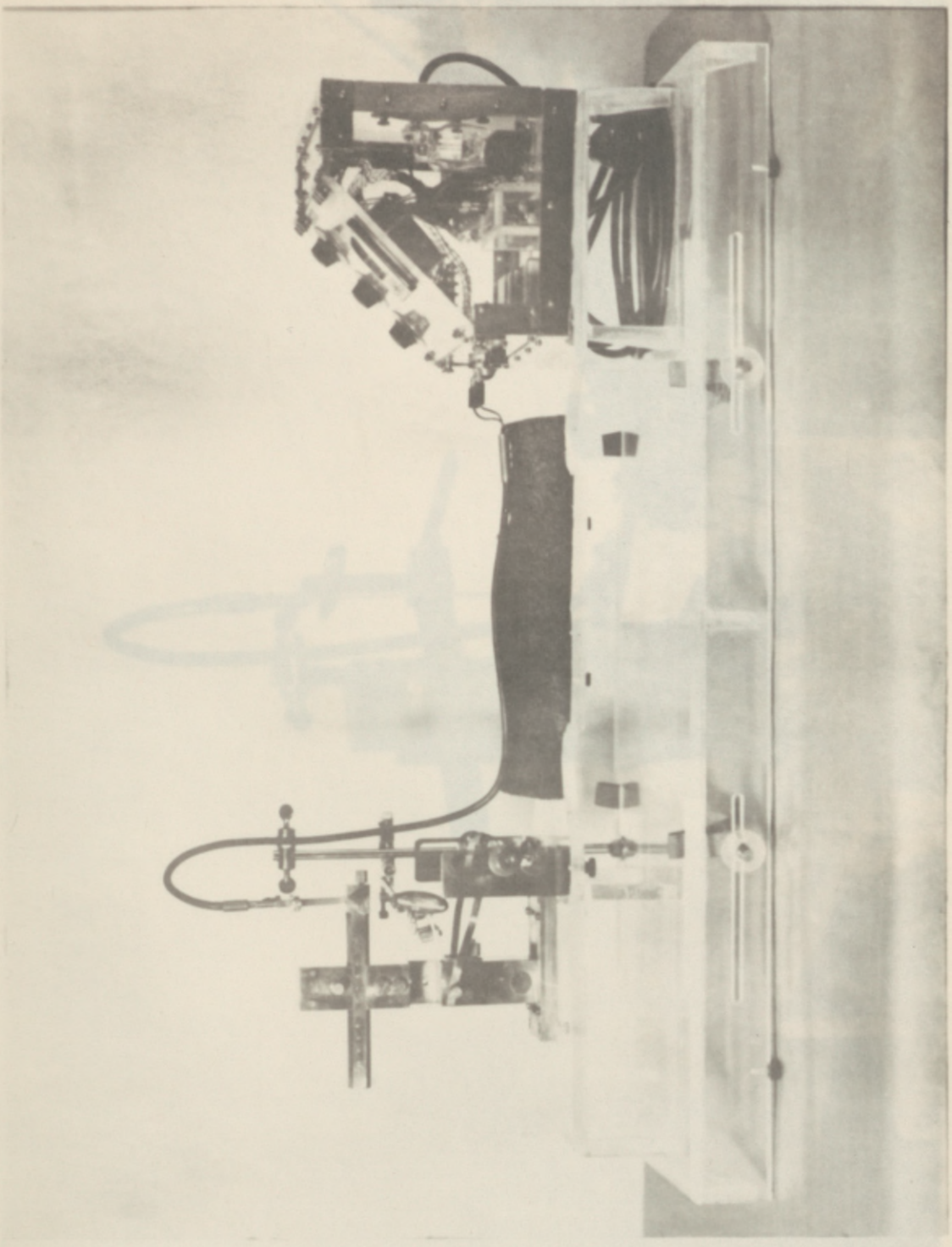

FIG. 1

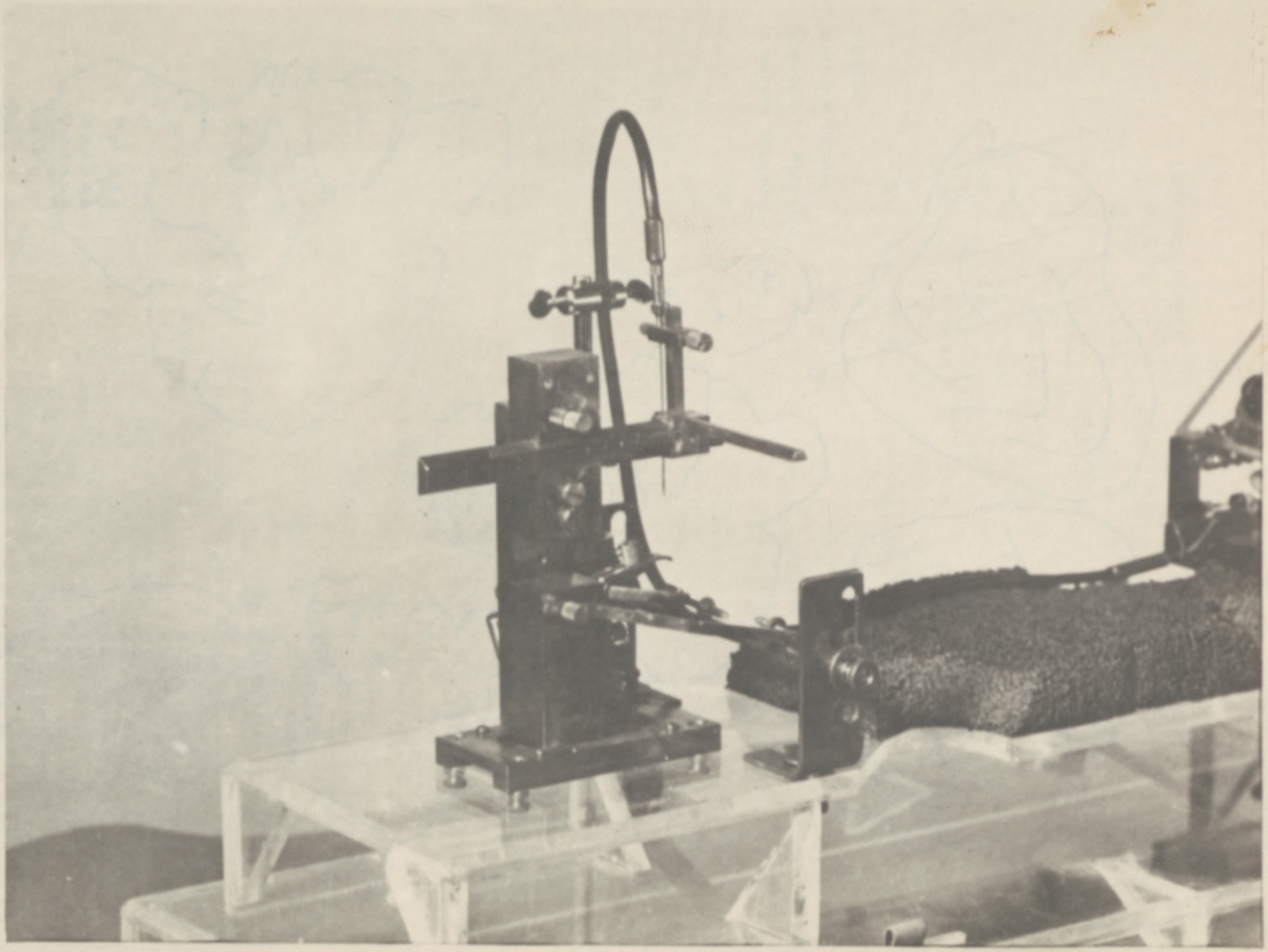

FIG. 2

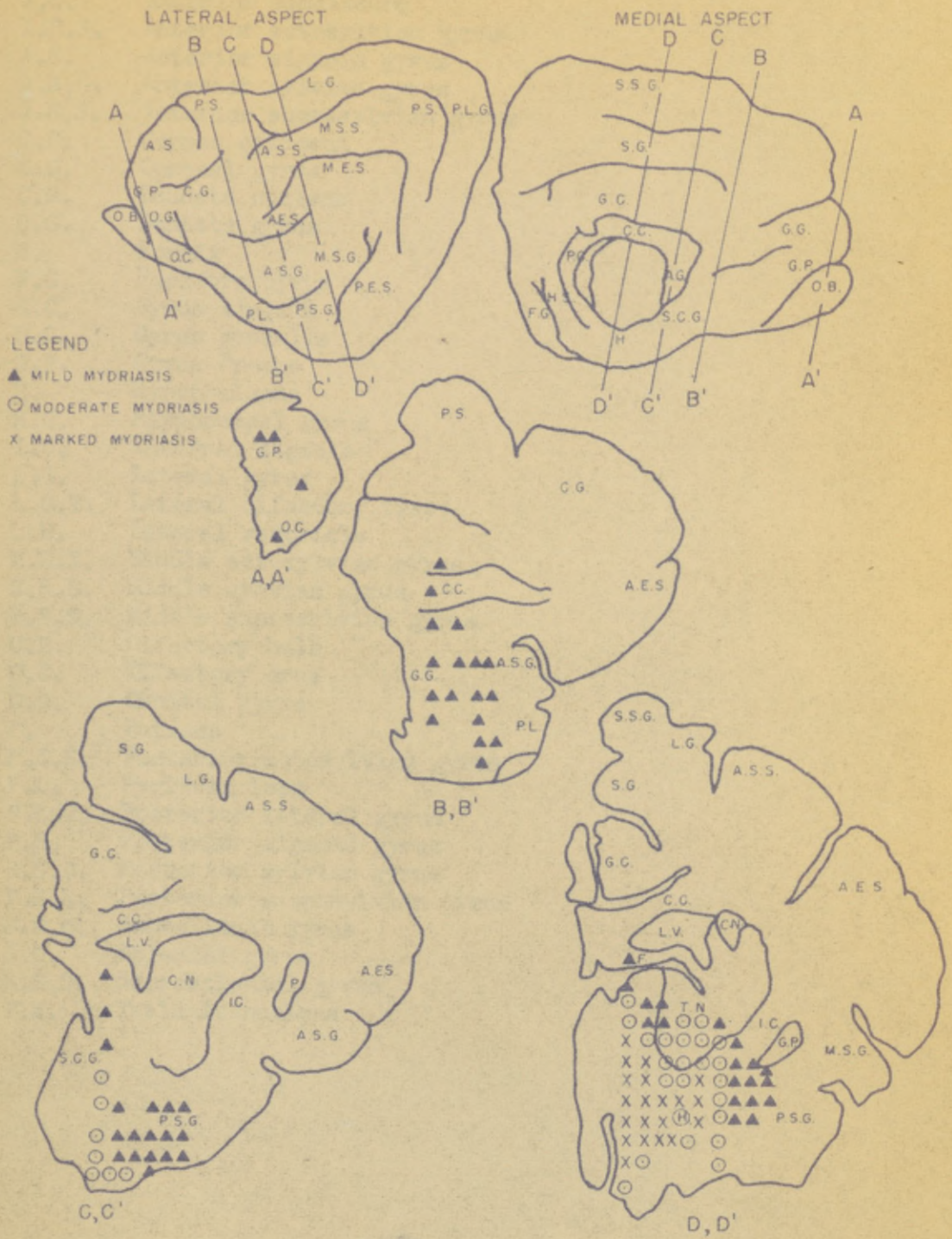
LATERAL ASPECT
MEDIAL ASPECT
LEGEND
▲ MILD MYDRIASIS
○ MODERATE MYDRIASIS
X MARKED MYDRIASIS
A,A'
B,B'
C,C'
D,D'

FIG. 3

KEY FOR FIGURE 3

A.C.	Anterior commissure
A.E.S.	Anterior ectosylvian gyrus
A.S.	Anterior sigmoid gyrus
A.S.G.	Anterior sylvian gyrus
A.S.S.	Anterior suprasylvian gyrus
C.C.	Corpus callosum
C.G.	Coronal gyrus
C.N.	Caudate nucleus
D.G.	Dentate gyrus
F.	Fornix
F.G.	Fusiform gyrus
G.C.	Gyrus cinguli
G.G.	Gyrus genualis
G.P.	Gyrus Proeus
H.	Hypothalamus
H.G.	Hippocampal gyrus
I.C.	Internal capsule
L.G.	Lateral gyrus
L.O.T.	Lateral olfactory tract
L.B.	Lateral ventricle
M.E.S.	Middle ectosylvian gyrus
M.S.G.	Middle sylvian gyrus
M.S.S.	Middle suprasylvian gyrus
O.B.	Olfactory bulb
O.C.	Olfactory crus
O.G.	Orbital gyrus
P.	Putamen
P.E.S.	Posterior ectosylvian gyrus
P.L.	Pyriform lobe
P.L.G.	Posterior lateral gyrus
P.S.	Posterior sigmoid gyrus
P.S.G.	Posterior sylvian gyrus
P.S.S.	Posterior suprasylvian gyrus
S.C.G.	Subcallosal gyrus
S.G.	Splenial gyrus
S.S.G.	Suprasplenial gyrus
T.N.	Thalamic nucleus

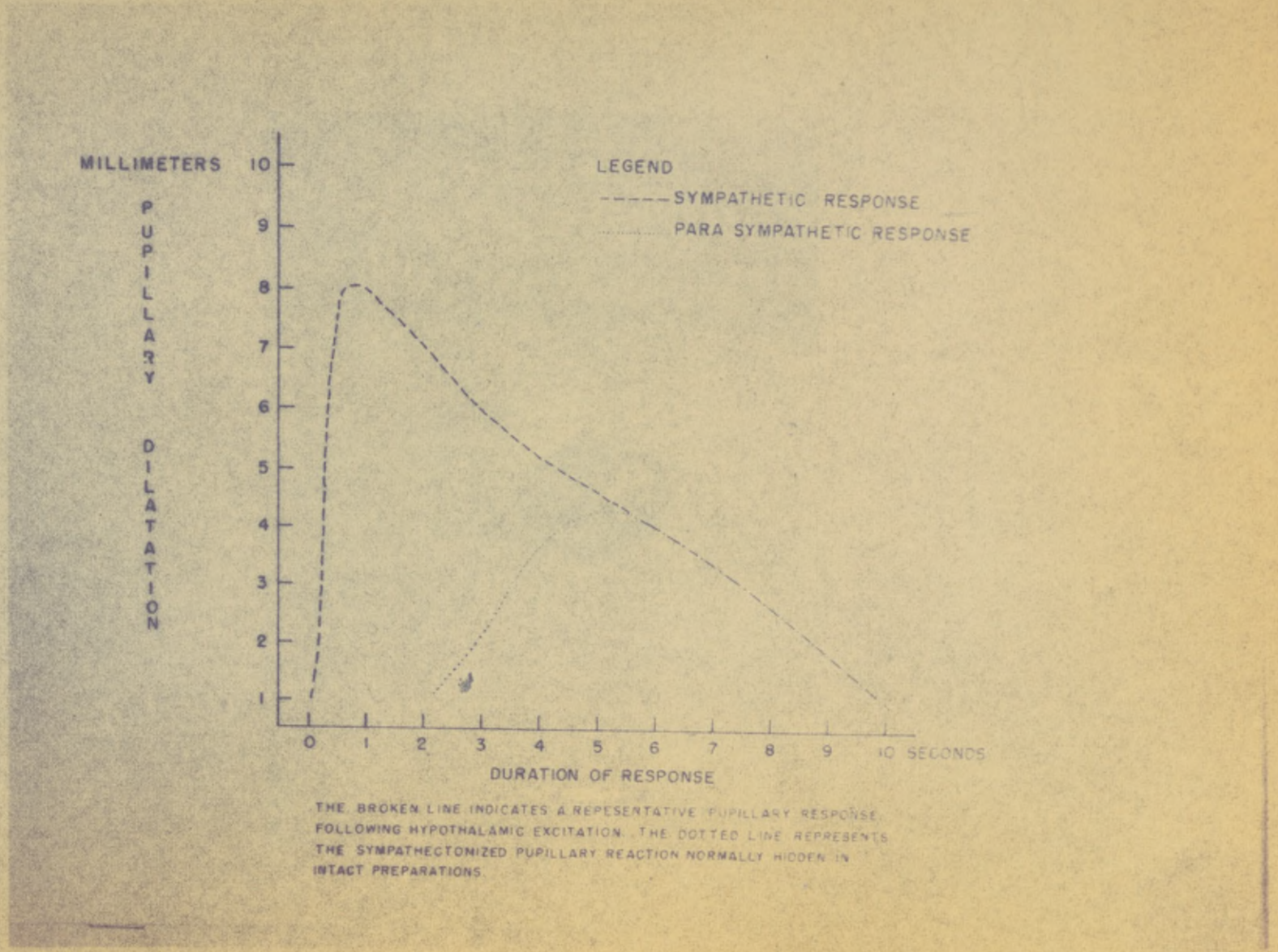
MILLIMETERS
PUPILLARY DILATATION
10
9
8
7
6
5
4
3
2
1
LEGEND
SYMPATHETIC RESPONSE
PARA SYMPATHETIC RESPONSE
0 1 2 3 4 5 6 7 8 9 10 SECONDS
DURATION OF RESPONSE
THE BROKEN LINE INDICATES A REPESENTATIVE PUPILLARY RESPONSE FOLLOWING HYPOTHALAMIC EXCITATION. THE DOTTED LINE REPRESENTS THE SYMPATHECTONIZED PUPILLARY REACTION NORMALLY HIDDEN IN INTACT PREPARATIONS.

FIG. 4

FIG. 5

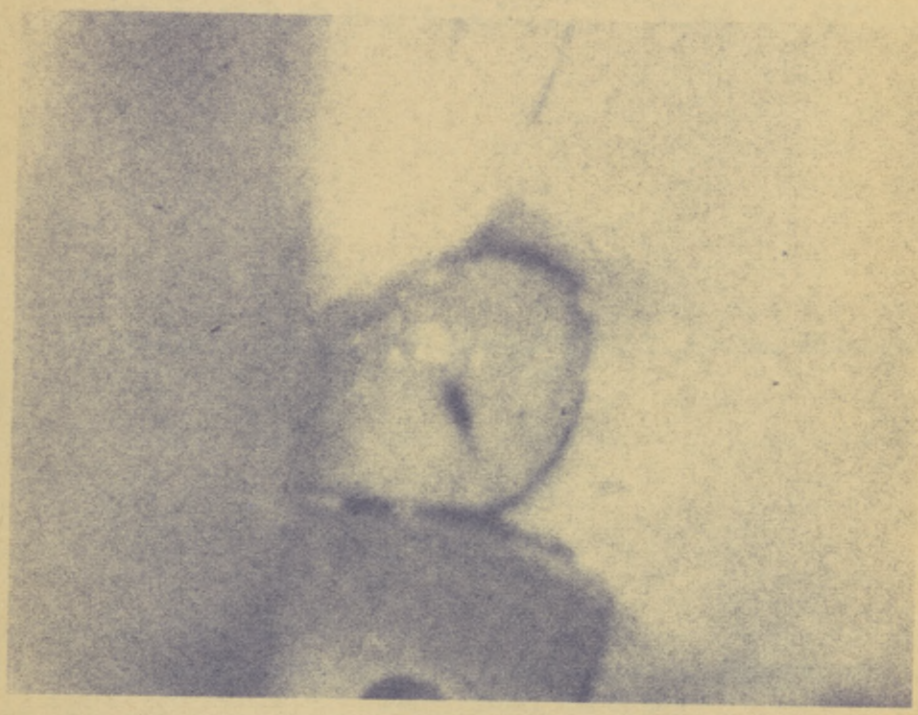

FIG. 6