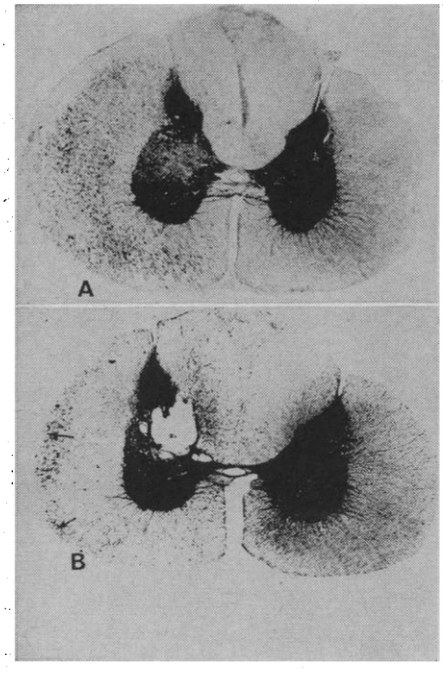

Fig. 1 (left). (A) Transverse section of spinal cord just rostral to a hemisection at C2 to C3. On the operated side many fibers stained for cholinesterase. To make these fibers clearly visible for photography, the sections were stained more heavily than usual. Thus the grey matter is over-stained. (B) Section just caudal to the lesion. The arrows point to fibers showing accumulation of cholinesterase in lateral and ventrolateral regions near the cord surface.

thetized with pentobarbitone were hemisected at C3, TI0, or L1; 6 to 7 days after the operation each animal was again anesthetized and was perfused with saline and then with 10 percent formol-saline. The spinal cord was removed and placed in 10 percent neutral formol-saline for 4 hours at 4°C. It was then washed in distilled water and immersed in 20 percent ethanol at 4°C. Serial sections (75 μ) were cut on a freezing microtome and incubated for 45 minutes at room temperature in acetate buffer (pH 5.9) or in the same buffer containing $10^{-7}M$ ethopropazine hydrochloride or $10^{-4}M$ [(3-oxopentamethylene)di-p-phenylene] bis [allyldimethyl–bromide (BW 284C51). The sections were then stained for cholinesterase according to a modification of the method of Gomori (*5*). Acetylthiocholine iodide was used as the substrate. The stained sections were washed, dehydrated, cleared, and were then mounted in neutral balsam.

A transverse section of the spinal cord just rostral to a hemisection at C2 to C3 is illustrated in Fig. 1A. There was an accumulation of cholinesterase in many fibers on the side of the lesion but no fibers cut in transverse section were stained on the unoperated side. Similar regions showed accumulation of cholinesterase following lesions at T10 and L1. The use of inhibitors showed that the enzyme was "specific" cholinesterase. Cholinesterase appeared to be localized in regions which carry fibers of the lateral corticospinal, rubrotegmentospinal, olivospinal, vestibulospinal, and reticulospinal tracts. It is difficult at this stage to be certain which of these tracts contain cholinesterase-staining fibers, but the results suggest that there may be many descending cholinergic fibers in the spinal cord.

A section just caudal to the lesion is shown in Fig. 1B. Fewer fibers were stained and the distribution of them was different from that found rostral to the lesion. Accumulation of cholinesterase occurred in two regions, lateral and ventro-lateral, near the surface of the cord and also in a few scattered fibers in the dorsal columns. This latter result was surprising but agrees with the observation, although in another species, that about 10 percent of the cells of the dorsal root ganglion stain for cholinesterase (*6*). The lateral and ventro-lateral accumulations were present at the three levels examined, and the former appears to be in the region of the ventral spinocerebellar tract. It is interesting to note that propriospinal regions surrounding the grey matter were unstained in both sections.

Precise identification of the ascending and descending cholinesterase-staining tracts must await further study.

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References and Notes

1. C. H. Sawyer, *Amer. J. Physiol.* **146**, 246 (1946); L. Lubińska, S. Niemierko, B. Oberfield, *Nature* **189**, 122 (1961) .
2. C. C. D. Shute and P. R. Lewis, *ibid.* **189**, 332 (1961); ———, *Bibliotheca Anat.* **2**, 34 (1961).
3. P. R. Lewis, C. C. D. Shute, A. Silver, *J. Physiol.* **172**, 9 P (1964); see also T. J. Biscoe and D. W. Straughan, *ibid.* **183**, 341 (1966).
4. C. C. D. Shute and P. R. Lewis, *Nature* **199**, 1160 (1963); K. Krnjević and A. Silver, *J. Anat. (Lond.)* **99**, 711 (1965); K. Krnjević and J. W. Phillis, *J. Physiol.* **166**, 296 (1963); J. W. Phillis and G. C. Chong, *Nature* **207**, 1253 (1965).
5. G. Gomori, in *Microscopic Histochemistry*, G. Gomori, Ed. (Univ. of Chicago Press, Chicago, 1952), pp. 210–12.
6. G. Filogamo and L. Candiollo, *Acta Anat.* **51**, 273 (1962).

16 May 1966

Interaction of Cortex and Superior Colliculus in Mediation of Visually Guided Behavior in the Cat

Abstract. *Total contralateral hemianopia follows unilateral removal of the entire occipito-temporal neocortex in the cat. This deficit is classically ascribed to interruption of visual radiations serving cortical function ("cortical blindness") and is considered permanent. Return of vision to the hemianopic field after subsequent removal of the superior colliculus contralateral to the cortical lesion demonstrates that neither assumption is correct. The initial hemianopia is apparently due to depression of function of the colliculus ipsilateral to the cortical lesion, a depression maintained by influx of inhibition from the crossed colliculus. Thus, removal of the contralateral tectum, or splitting of the collicular commissure, abolishes this inhibition and allows the return of function in the ipsilateral colliculus, and with it the recovery from hemianopia. These findings emphasize that visually guided behavior is mediated at both cortical and midbrain levels, and that there is a marked interaction between these sites.*

Visual fields of the cat can be ascertained and measured rather accurately by means of a simple perimetric test in which animals are trained to fixate and to respond to food stimuli. When tested in this fashion with monocular masks, the horizontal visual field of each eye includes about 130°, that is, the field of the right eye extends from 100° right to 30° left of fixation. The area of binocular overlap so measured (60°) is somewhat reduced from the actual amount by presence of the mask. Field deficits after lesions can be measured with an accuracy of about 10°. After recovery or compensation of a field deficit, bilateral stimulation can demonstrate inattention or neglect of one visual field by preferential response to stimuli in the opposite field. This and other "clinical" behavioral tests for deficits

in visually guided behavior (following of moving stimuli, blink to threat, placing, depth perception in jumping and avoidance of obstacles, and choice of food-baited plaques placed on opposite sides of a runway) have been used and are described in detail elsewhere (*1*).

Deficits in visually guided behavior, measured in these ways, follow unilateral removal of the superior colliculus (*1*) and of various areas of the occipito-temporal cortex (*2*). Unilateral colliculectomy which does not invade the pretectum or the underlying tegmentum results initially in contralateral homonymous hemianopia complete to the vertical meridians, marked ipsiversive circling, and a deficit in contralateral movements of the eyes, although compensation occurs in all of these changes in the succeeding several weeks. Responses to stimuli in the contralateral fields appear gradually, beginning at the midline and extending to about 60° lateral; between 60° and 100° responses are irregular and when present are slow. Simultaneous bilateral stimulation always results in response to the ipsilateral side, even when the contralateral stimulus is larger and has greater movement. Tactile and acoustic deficits also occur in this preparation (*1*).

Alteration in visual behavior after various unilateral cortical lesions in the cat has been thoroughly described (*2*), together with the resulting thalamic degeneration. Removal of the striate cortex (area 17), largely sparing areas 18 and 19 (see Fig. 1), results in only minimal and transient deficits or in no deficit at all. Progressively larger occipito-temporal ablations, which in addition to the striate cortex include areas 18 and 19 and the middle and posterior suprasylvian gyri (with severe atrophy of the dorsal lateral geniculate nucleus), result in deficits which when compensated are similar to those that occur after colliculectomy. Only when the lesion includes all of these areas plus the auditory cortex and temporal fields (that is, extends from the splenial sulcus to or near the rhinal fissure, Fig. 2) is the deficit one of contralateral hemianopia complete to, or within a few degrees (< 10°) of, the vertical meridians (*3*). Except for this evidence of macular sparing, the half-field blindness was total and showed no compensation during survival periods up to 1 year in six cats. The importance of completeness of the lesions is shown by other animals, in which sparing of only part of the striate cortex or the middle suprasylvian gyrus resulted in considerable recovery. In contrast, unilateral removal of the frontal cortex resulted in no visual deficits (*2*). Thus, cortex lying outside of the classically defined first (area 17) and second (areas 18 and 19) visual fields make a significant contribution to the mediation of visually guided behavior. This conclusion is in agreement with the conclusions of others who used pattern and intensity discrimination tests (*4*).

From these results it is apparent

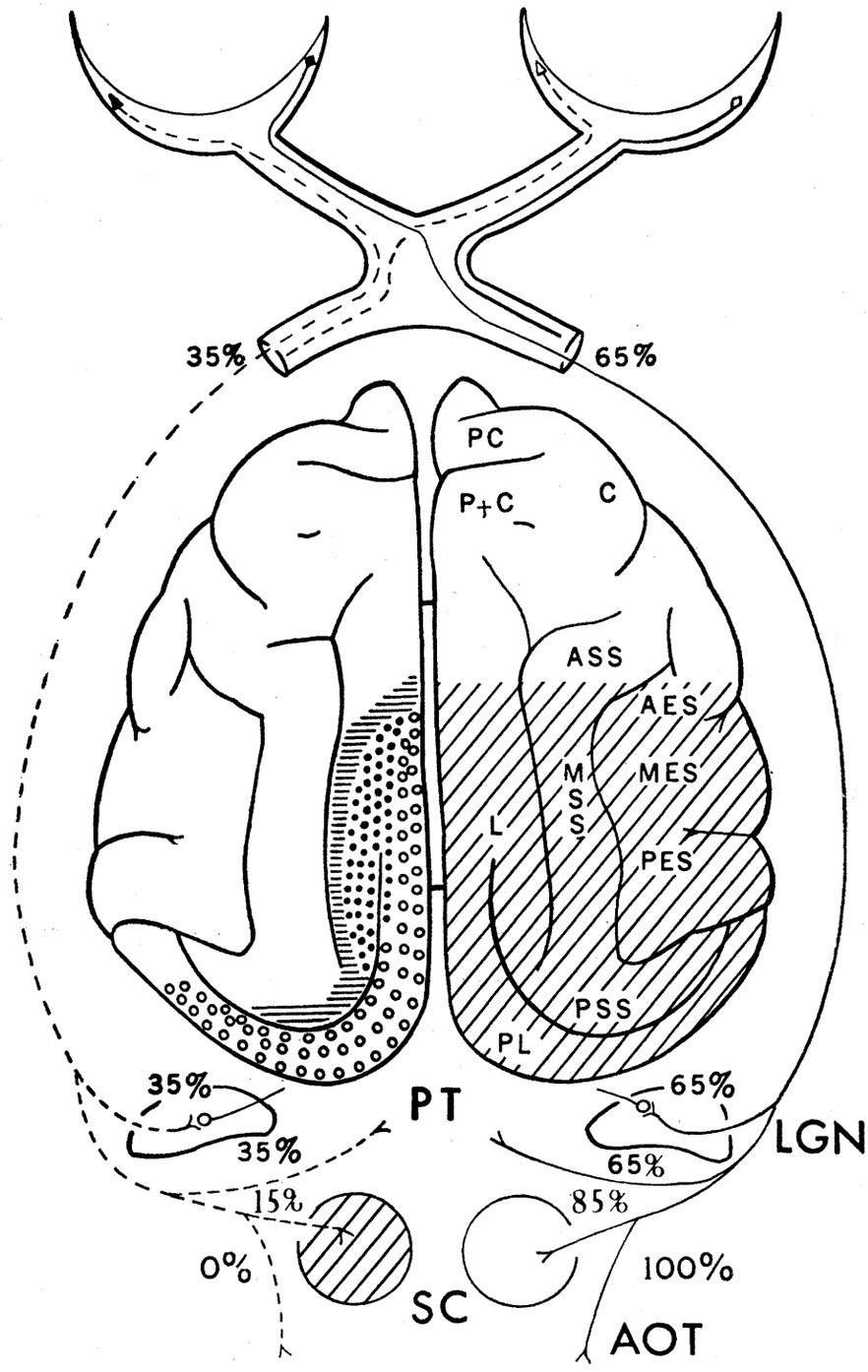

Fig. 1. Schematic drawing to show the primary visual pathways in the cat. The approximate percentage of crossed and uncrossed fibers, based on estimates from anatomical studies (*7*), is shown at the level of the optic chiasm, the lateral geniculate nucleus (*LGN*), pretectum (*PT*), superior colliculus (*SC*), and accessory optic system (*AOT*). Note that the percentages present at the chiasm are maintained at *LGN* and *PT*, but not at *SC* and *AOT*. Diagonal hatching in the right cortex and left colliculus indicates the crossed lesions described in the text. Symbols plotted on the left cortex show the topography of area 17 (circles), 18 (dots), and 19 (lines), taken from Otsuka and Hassler (*8*).

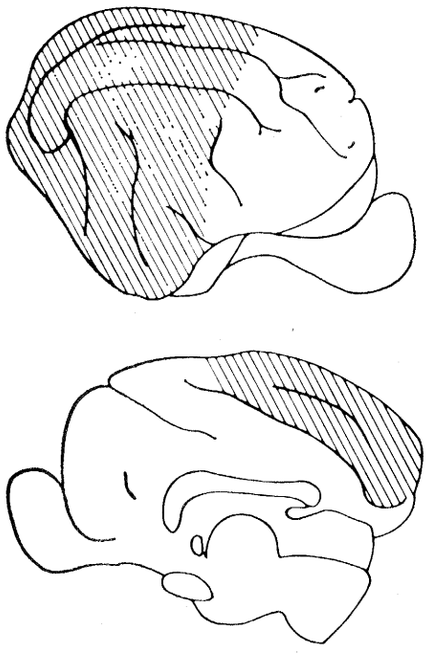

Fig. 2. Drawings of the lateral and medial aspects of the cat's brain to show the extent of removal of occipito-temporal cortex that results in total hemianopia.

that visually directed behavior is mediated at both cortical and midbrain sites, and it is the purpose of this report to describe the interaction between these two levels of the brain which can be seen after sequential chronic lesions. Thus, after full compensation and stabilization of deficits following subtotal occipito-temporal cortical lesion, the ipsilateral colliculus was removed, while in other animals the sequence was reversed. When the two lesions were placed on the *same side* of the brain, partial contralateral field deficits, residual after the first lesion, were converted into total hemianopia as a result of the second lesion, regardless of the sequence. This marked potentiation was found when the cortical lesion involved areas 17, 18, and 19 and the middle and posterior suprasylvian gyri, or area 17 alone, and the ensuing total hemianopia showed no further compensation, provided area 17 was completely removed and the colliculus largely destroyed in each case. No potentiation of the collicular deficit was found after removal of the frontal cortex. Thus, despite the obvious contribution of extrastriate cortex in the mediation of visually guided behavior, this cortex is not capable of functional compensation in the absence of area 17 and the superior colliculus.

When cortical and tectal lesions are placed sequentially on *opposite sides* of the brain, the resultant effects do not summate but instead are opposed. This process is dramatically shown by first removing the entire right occipito-temporal cortex from splenial sulcus to rhinal fissure, a lesion that results in total hemianopia of the left fields (Figs. 1 and 2). Despite vigorous training of these animals for extended post-operative periods up to 1 year, no compensation of this deficit was discernible. This deficit represents the end-point in the severity of visual loss caused by a unilateral lesion. After subsequent removal of the left colliculus contralateral to the cortical lesion, marked changes were apparent as soon as animals recovered from anesthesia. Table 1 shows the nature of these changes in one animal (cat 73) with almost complete collicular removal (Fig. 3). Thus visual responses returned to the previously hemianopic left fields (*5*). The initial deficit induced in previously normal right fields by the tectal lesion was expected from previous studies (see *1*) but was less marked than that seen in animals with only tectal lesions.

After compensation the responses to the peripheral fields of both sides were similar; they were slower than in the normal cat and were evoked only by moving stimuli. Only those stimuli near the midline evoked brisk responses and only here were responses obtained to stationary objects. This field of maximal acuity lay within the area of binocular overlap and extended somewhat more lateral on the right side (30°) than on the left (10°). Two other cats gave similar results but showed recovery of responses to stimuli in the left visual fields only to 60°; in one of these (cat V8), with histology available, the lesion was limited to the caudal two-thirds of the colliculus with sparing of the lateral part in much of the lesion area (Fig. 4). The neural state of these animals can be understood by reference to Fig. 1, in which these two lesions are indicated by diagonal hatching. It will be seen that responses to stimuli in the right visual fields are mediated by the intact left hemisphere, while responses to the left side are mediated by the intact right

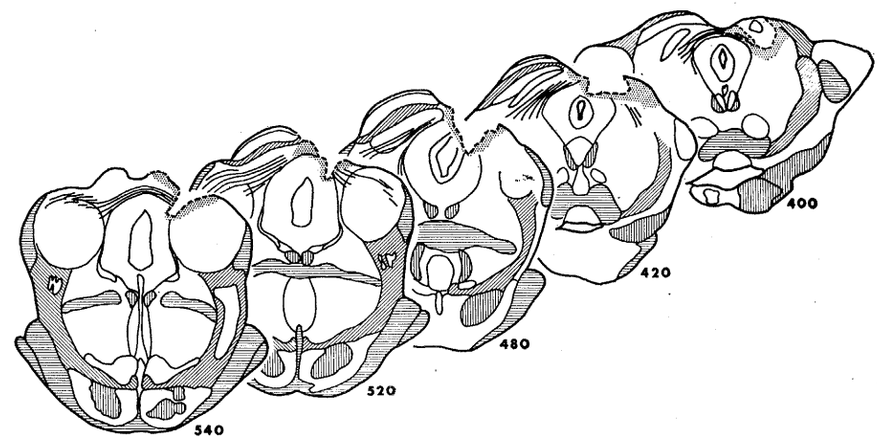

Fig. 3. Drawings of selected sections to show extent of the lesion in the superior colliculus in cat 73. Area of total destruction enclosed by dashed lines; partial cell and fiber loss indicated by dots.

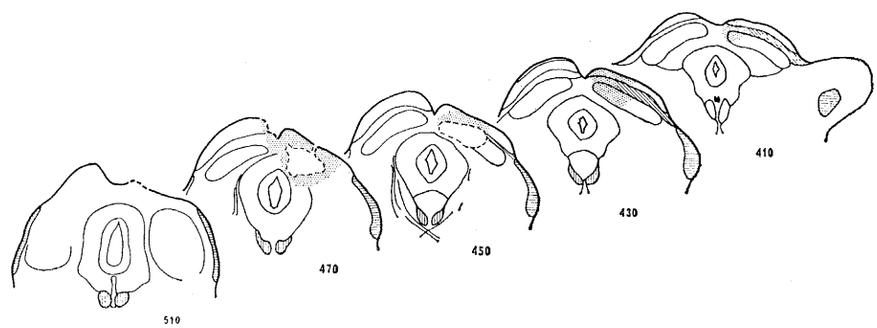

Fig. 4. Drawings of selected sections to show the extent of the lesion in the superior colliculus in cat V8.

Table 1. Summary of visual deficits that follow cortical lesion and the changes that occur after subsequent removal of the contralateral superior colliculus.

Deficits after right cortical lesion	Deficits after subsequent lesion in left superior colliculus
Total hemianopia left fields	Response to stimuli in left fields (0° to 100°)
Normal right fields (0° to 100°)	Response to stimuli in right fields 0° to 45° initially, improving slowly to 70°, then to 100°
Following only to right	Following only to left initially, slowly appearing on right, but left favored
Blink to lateral threat only on right	Blink to threat initially only on left, slowly appearing on right
Lateral visual placing only on right	Placing initially on left, slowly appearing on right
Tendency to circle right	Marked initial circling to the left, slowly reduced to tendency to circle left
Eye movements and pupils normal	Pupils normal; eye movements to right initially absent, slowly improving to almost normal, slightly better to left

superior colliculus and possibly other midbrain structures. After time is allowed for stabilization, a rather remarkable balance is seen between left cortex and right colliculus in control of the visual behavior as measured here.

In attempting to understand the neural mechanisms underlying these changes, one must ask this question: In view of the active participation of the superior colliculus in visually guided behavior, why, after the initial cortical lesion, is the ipsilateral colliculus not functioning for the hemiretinae which project to it "look" directly into the hemianopic field (see Fig. 1)? Apparently this colliculus is functionally depressed, either because of removal of facilitation mediated by corticotectal fibers (*6*) or because of an inhibition resulting from imbalance of visual centers after the cortical lesion, or both. Since subsequent ablation of the contralateral colliculus returns visual responses to the previously hemianopic fields, one may assume that (i) this phenomenon is due to recovery of function of the ipsilateral colliculus and (ii) this recovery is the result of removal of an inhibition that emanates from the tectum of the opposite side.

If the hypothesis of a crossed tectal inhibitory influence is correct, then splitting the commissure of the superior colliculus should be as effective as removal of the colliculus contralateral to the cortical lesion. This proved to be the case in two animals. In one (cat V3), in which the lesion was limited to caudal one-half of the collicular commissure, responses appeared to the left visual fields 3 weeks after commissurotomy. Recovery began at the midline (vertical meridian) and by 10 weeks included the full field of 100°; apart from mild pupillary dilatation and sluggishness of response to light, other signs which follow colliculectomy (Table 1) were absent. In the other cat, which was not killed but which had more extensive tectal split that apparently extended into the pretectum (evidenced by maximal pupillary dilatation), recovery of responses to the left were first observed at 6 weeks, again beginning at the vertical meridian, and by 16 weeks had extended to 60°. Delay in the return of vision to the previously hemianopic fields after tectal commissurotomy, in contrast to the immediate recovery after collicular ablation, should be pointed out, although I have no immediate explanation.

The hemianopia that follows unilateral removal of the cortex that mediates visual behavior cannot be explained simply in classical terms of interruption of the visual radiations that serve cortical function. Explanation of this deficit requires a broader point of view, namely, that visual attention and perception are mediated at both forebrain and midbrain levels, which interact in their control of visually guided behavior. Hemianopia caused by cortical lesion is due to an imbalance of these neural centers that subserve vision, resulting in an alteration of function at the midbrain level. Imbalance can be redressed and vision restored to the previously hemianopic field by subsequent lesion in the superior colliculus.

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References and Notes

1. J. M. Sprague and T. H. Meikle, Jr., *Exp. Neurol.* **11**, 115 (1965).
2. J. M. Sprague, in *The Thalamus*, D. P. Purpura and M. D. Yahr, Eds. (Columbia Univ. Press, New York, 1966).
3. These observations are probably related to the fact that in the cat the lateral geniculate nucleus projects to cortical fields outside of area 17 [see *2*, T. H. Meikle, Jr., and J. M. Sprague, *Int. Rev. Neurobiol.* **6**, 149 (1964), and L. J. Garey, *Nature* **207**, 1410 (1965)].
4. R. E. Myers and R. W. Sperry, *Arch. Neurol. Psychiat.* **80**, 298 (1958); R. W. Sperry, R. E. Myers, A. M. Schrier, *Quart. J. Exp. Psychol.* **12**, 65 (1960); T. Gualtierotti, *Amer. J. Physiol.* **200**, 1215 (1961); P. M. Meyer, *J. Comp. Physiol. Psychol.* **56**, 397 (1963); J. P. Baden, J. C. Urbaitis, T. H. Meikle, Jr., *Exp. Neurol.* **13**, 233 (1965).
5. One animal was prepared with unilateral removal of all cortex, rhinencephalon, and basal ganglia; visual deficits were similar to those shown on the left side of Table 1. After 1 year the contralateral colliculus was completely removed and there followed a delayed (6 weeks) and partial (30°) recovery of responses to the previously hemianopic fields. The cat was killed soon after so that further extension of this field cannot be ruled out.
6. D. Jassik-Gerschenfeld, P. Ascher, J. A. Guevara, *Arch. Ital. Biol.* **104**, 30 (1966).
7. A. M. Laties and J. M. Sprague, *J. Comp. Neurol.*, in press.
8. R. Otsuka and R. Hassler, *Arch. Psychiat. Ztschr. Neurol.* **203**, 212 (1962).
9. Supported in part by research grant NG-05506 from NIH.

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Long Temporal Gradient of Retrograde Amnesia for a Well-Discriminated Stimulus

Abstract. *This experiment tested the general validity of recent findings that retrograde amnesia can be produced by electroconvulsive shock only if the shock is administered within 10 to 30 seconds after the learning trial. Precautions were taken to avoid confusion of other shock effects with retrograde amnesia. A temporal gradient of electroconvulsive shock-produced retrograde amnesia, extending up to at least 1 hour, for a well-discriminated stimulus, was demonstrated in mice in a one-trial learning passive avoidance situation.*

Recently Quartermain *et al.* (*1*) reported that retrograde amnesia could be produced in rats by electroconvulsive shock (ECS) if the shock was administered within 30 seconds after a learning experience, but not later. The brevity of this temporal gradient strongly substantiated findings of Chorover and Schiller (*2*), who were unable to obtain any retrograde amnesic effect from ECS administered more than 10 seconds after the learning trial.

Quartermain *et al.* (*1*) suggest that retention deficits after much longer ECS delays, as reported by other investigators (*3*, *4*) may be the results of different task and procedural variables. They point out that studies which have shown significant effects of ECS ad-