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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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-

ministered after long delays have generally used learning tasks in which the subjects have received considerable training under deprivation of food or water before the punishing shock was administered.

Chorover and Schiller (*5*) offer an alternative explanation for ECS effects observed when ECS is administered more than 10 seconds after one-trial passive avoidance learning, referring to an effect upon "the locomotor inhibitive component of a generalized conditioned emotional response (CER)" established in the course of the learning procedure. They feel that if certain precautions are taken in a passive avoidance test this CER component can be minimized and that under such circumstances ECS has no effect on retest performance if administered more than 10 seconds after the training trial. They seem to imply that this effect of ECS on the CER shows no temporal gradient.

The findings of Chorover and Schiller (*2*) and Quartermain *et al.* (*1*) cast doubt on results of investigators who have reported ECS effects on retest performance after delays much longer than 10 to 30 seconds (*3, 4*). If the effect of an ECS administered after a long delay were due to an effect on a "generalized CER" established in the course of the learning procedure [as suggested by Chorover and Schiller (*4*), implying that this effect on retest latencies had nothing to do with retrograde amnesia], the interpretations of the results of investigators reporting such ECS effects after long delays would have to be seriously questioned.

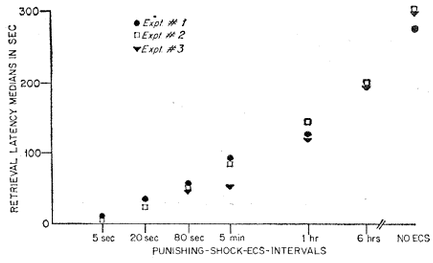

Fig. 1. The temporal gradient of retrograde amnesia following ECS in mice. Every symbol represents the retrieval test latency median of 7 to 8 animals.

The present experiment was designed to test the general validity of the findings of Chorover and Schiller (*2*) and Quartermain *et al.* (*1*), taking the precautions recommended by these authors to avoid confusion of other ECS effects with retrograde amnesia, especially in the case of a long delay. In determining the time within which retrograde effects of an ECS could be obtained in a one-trial learning situation we used animals that had not been subjected to pretraining and ascertained that the avoidance response produced by the punishing shock was discriminatory.

Female CF1 mice approximately 60 days of age were trained in a two-chambered box where they could receive a single punishing shock [800 volts a-c through 2 megohms in series causing approximately 320 μa root mean square (r.m.s.) $\pm$ 15 percent flow through the animal for 0.8 second] for stepping spontaneously from a small lighted compartment into a larger darkened one. This one-trial learning procedure (registration) generally took less than 20 seconds. Electroconvulsive shock (800 volts a-c through 40 kohm in series causing approximately 15 ma r.m.s. $\pm$ 20 percent to flow through the animal for 0.2 second) producing full tonic seizures was administered outside the apparatus, transcorneally, to different groups of mice, 5, 20, 80, 320 seconds, 1 hour, or 6 hours after learning. A control group received no ECS after registration. A second control group received no punishing shock but ECS. Approximately 24 hours after the learning trial the animals were again placed in the brightly lighted compartment for retest and the latencies of stepping into the darkened chamber were measured (retrieval test). Animals tarrying longer than 300 seconds were removed.

It is clear from Fig. 1, which is based on three independent experiments, that the longer the ECS treatment is delayed the smaller is its effect upon a subsequent retrieval trial. Table 1 contains the pooled data of three experiments. It can be seen that the difference between 5 minutes and 1 hour is still significant ($p < 0.01$) (*6*). The difference between 1 hour and 6 hours just misses significance ($p > 0.05$). The difference between the latencies of the 6-hour group and of the control group receiving punishing shock without ECS is significant ($p < 0.01$). Table 1 includes a control group which did not receive a punishing shock in the step-through box but which received a single ECS outside the box 10 seconds after having stepped into the second compartment. The low retest latencies indicate that the single ECS is not punishing.

These results support the view that consolidation processes may extend

Table 1. Retest latency decrements when ECS was given at different intervals after learning. N.S., not significant.

ECS administered after learning trial	Mice (No.)	Retest latency medians (sec)	Interquartile range (sec)	Probabilities of differences between groups
5 seconds	16	9.3	6.3 to 16.2	
				$p < 0.005$
20 seconds*	16	27.8	17.6 to 46.2	
				$p < 0.025$
80 seconds	23	50.3	36.5 to 87.0	
				N.S.
320 seconds*	23	82.8	35.3 to 119.0	
				$p < 0.01$
1 hour	23	127.7	97.3 to 174.9	
				N.S.
6 hours*	16	195.0	98.6 to 251.6	
				$p < 0.01$
No ECS	24	>300.0	188.0 to >300.0	
No punishing shock; ECS 10 seconds after stepping through	9	5.0	3.5 to 11.1	

* Twenty seconds versus 320 seconds: $p < 0.005$; 320 seconds versus 6 hours: $p < 0.005$.

Table 2. Effect of punishment, inside the apparatus versus outside, on retest latencies.

Group	Received punishing shock	Mice (No.)	Median of retest latencies (sec)	Interquartile range (sec)
A	Inside box	9	290.5	216.4 to >300
B	Outside box	25	7.0	5.8 to 20
C	No punishing shock	24	6.7	4.3 to 13.6

over minutes and perhaps even hours or days (*3, 4, 7*). The discrepancy between our results and those of Chorover and Schiller (*2*) and Quartermain *et al.* (*1*) may be related to different species used (rats versus mice) or to the intensity of the punishing shock. There is a suggestion in the data of Chorover and Schiller (*2*) that a retrograde amnesic effect may have been produced by ECS administered 30 seconds after foot shock when the duration of the punishing shock was diminished to 0.5 second.

Beyond 1 hour the gradient appears to level off and differences between groups that received ECS 1 and 6 hours after the learning trial versus unconvulsed animals may be due to a proactive disinhibitive effect of the ECS on retrieval test performance. The time course of proactive disinhibitive effects of ECS cannot be determined from the present results.

In order to check the possibility suggested by Chorover and Schiller (*5*) that ECS effects obtained after long delays might be due to an action on a generalized CER established in the course of the learning trial, we examined the generalizability of the punishment. A group of animals was trained in the apparatus in the usual way, except that upon stepping into the inner compartment they were immediately removed and put into a small restraining device, an electrode was applied to the base of the tail, and a strong electric shock was administered (800 volts a-c through 40 kohm in series causing approximately 2.5 ma r.m.s. ± 30 percent to flow through the animal for 0.8 second). Under these conditions all animals squeaked and appeared to experience intense pain. It can be seen in Table 2 that group B, which received such a strong punishment outside the box, showed retest latencies that were essentially the same as those of unpunished control animals (group C) and were significantly lower ($p < 0.005$) than those of animals shocked in the box (group A). This indicates that the mice discriminated the stimuli of the avoidance situation and it implies that ECS lowered retest latencies by producing retrograde amnesia to a well-discriminated painful experience.

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22 April 1966

Insulated Gate Field Effect Transistor Amplifier

Rapid progress in semiconductor technology has made available devices that are well suited for use in specialized types of biological instrumentation. Junction gate and insulated gate field effect transistors (FET's) are examples of such devices, and each can be used in simple amplifier and other circuits that feature high input reactance, relatively low noise, and high gain (see *1*).

An inexpensive, miniature d-c electrometer-type amplifier was designed and built with the newest of these commercially available devices, the insulated gate field effect transistor (IGFET). Its characteristics make it especially useful for recording small biopotentials through high-resistance microelectrodes. The IGFET amplifier circuit (Fig. 1), its specifications, and some comparisons with other amplifiers are presented here.

The amplifier is 4 by 4 by 2 cm (another unit is a little larger than a cigarette), costs $36, and took 4 hours to build with standard components. The circuit uses an unbiased IGFET as the input stage which, although simple, still allows linear amplification of large (1 to 2 volts) or small (50 μv) positive or negative signals. This is not possible with other types of transistors.

The overall gain is 15 and it is developed in the first stage for maximum signal-to-noise ratio. Gain can easily be increased to 100 or more with a few simple component changes. Input resistance is 10^{13} ohm, output resistance is 6 kohm, and uncompensated input capacitance is between 1 and 4 picofarads. Input equivalent noise is about 2.5 db at 1 kc/sec with an input resistance between 4 and 10 Mohm. Although this noise figure is slightly higher than that of many IGFET's and "low-noise" conventional transistors, it is unique in that it occurs in the resistance range of microelectrodes that are used in many types of electrophysiological experiments.

The amplifier stages are directly coupled with simple resistor networks, and only two power sources are used. The latter should be mercury batteries for minimal long-term drift. Input

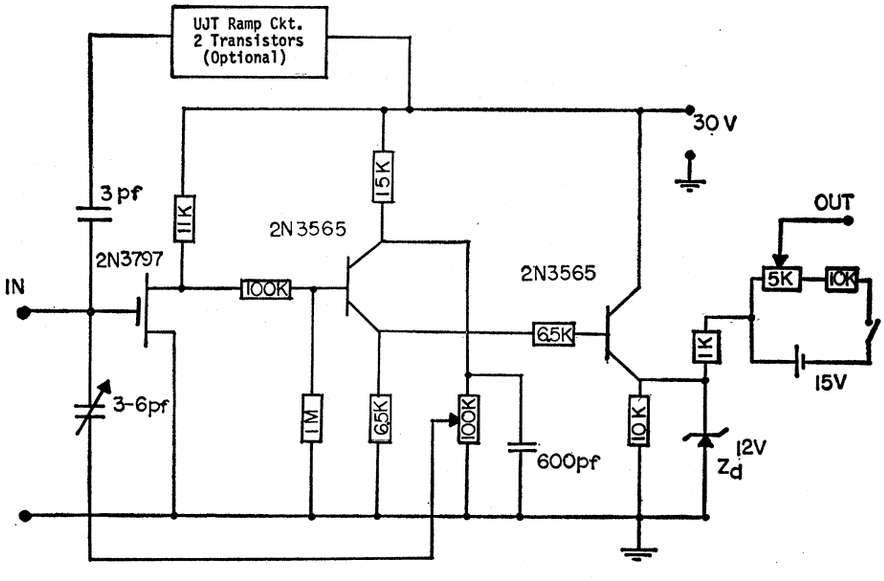

Fig. 1. Schematic diagram of the IGFET amplifier. For resistance values, $K = 1$ kohm. The UJT ramp circuit is used to check electrode resistance *in situ*. The 2N3565 are low-noise transistors operated at unity gain. Negative capacitance compensation is provided by the variable capacitor.