wave believed to be associated with function of the nonspecific sensory system. Similarly, lesions of the lateral geniculate body were made in an attempt to remove the short-latency, positive-negative wave complex believed to be related to specific visual function. Lesions were made electrolytically by stereotaxic control and also by aspiration under direct observation.

Lesions in the superior colliculus and pretectal area in kittens aged 9, 13, 15, and 17 days in all cases abolished or markedly diminished only the long-latency negative wave associated with the nonspecific visual system. Lesions in the lateral geniculate body in kittens aged 13, 15, and 16 days in all cases removed or greatly diminished only the short-latency waves associated with the specific visual system.

Figure 2 illustrates how both of these results were obtained in a 15-day-old kitten. The right eye (*A* to *D*) and the left eye (*E* to *H*) were stimulated separately with flashes of light; in each instance, only the tracing from the contralateral visual cortex showed a full complement of the components of the visually evoked response which have been observed at this age, including the long-latency negative wave of early origin and the positive-negative wave complex of shorter latency which appears subsequently. The short-latency positive component in a kitten of this age is usually absent or of low amplitude in the tracing from the ipsilateral visual cortex.

Columns 1 and 2 of Fig. 2 show typical visually evoked responses before (*A* and *E*) and after (*B* and *F*) operative exposure (*J*) of the fields where lesions are to be made. The control records (*B* and *F*) are not appreciably different from the initial records (*A* and *E*). Successive, two-stage ablations were made of (i) the right superior colliculus and pretectal region of the midbrain (*K*) and (ii) the right lateral geniculate body (*L*), by aspiration, under direct visual observation, through the lateral approach shown in *J*. In records *C* and *G*, made after removal of the right superior colliculus, the long-latency negative wave in the trace (*R*6) for the right visual cortex is abolished or markedly diminished but that in the trace (*L*5) for the left visual cortex is not. The short-latency, negative wave in *R*6 of *C*, and the positive-negative complex in *R*6 of *G* are relatively unaffected. In records *D* and *H*, after subsequent removal of the right lateral geniculate body, the short-latency negative component seen in *R*6 in *A*, *B*, and *C* and the short-latency positive-negative components seen in *R*6 in *E*, *F*, and *G* are removed only in the tracings (*R*6 in *D* and *H*) from the visual cortex on the side of the lesion.

Thus, a lesion of the right superior colliculus abolished or diminished the long-latency negative wave from the cortex on the side of the lesion when either eye was stimulated but did not affect the short-latency positive or negative components. A lesion of the right lateral geniculate body abolished the short-latency negative wave in the trace (*R*6) from the right visual cortex, with either right-eye (*D*) or left-eye (*H*) stimulation. Also, after this lesion, the positive wave component, which in *E*, *F*, and *G* occurred only in the trace (*R*6) from the visual cortex on the side opposite to stimulation, was absent from the trace (*R*6 in *H*) from the right visual cortex when the left eye was stimulated.

Therefore, the long-latency negative wave which appears first as the animal develops and which has been hypothesized to be a nonspecific sensory component, is blocked by a lesion of the superior colliculus and pretectal region. (It was not appreciably affected in several animals with only lesions of the lateral geniculate body.) Conversely, the short-latency positive-negative components are affected only by lesions of the lateral geniculate body and not by lesions of the superior colliculus and pretectum. Accordingly, these positive-negative components are attributed to the specific visual system.

Such a differentiation of electrocortical evoked responses into components associated with specific and nonspecific systems was aided by the serial recordings which reflected maturational changes and showed a separation of these system components at early ages. Further electrical and behavioral investigation of the visual modality in kittens is under way in an effort to clarify the development and interaction of specific and nonspecific visual systems, and to more clearly delineate their pathways and mechanisms.

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8 February 1965

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Facilitation: Electrical Response Enhanced by Conditional Excitation of Cerebral Cortex

Abstract. *Cats were conditioned to give a foot flexion in response to stimulation of the brain through implanted electrodes. The evoked electrical activity of an extracallosal interhemispheric pathway was much greater in the repeatedly stimulated direction than in the unstimulated direction in the brain. No difference in the two directions was observed in control animals that did not receive the unconditional foot shock.*

Changes have been reported in electroencephalograms (EEG) and evoked potentials obtained during short-term conditioning experiments. The report of Galambos and Sheatz (*1*) is especially noteworthy. Unfortunately, the reported changes in amplitudes of evoked potentials and in wave frequencies of EEG's as related to a conditioned behavior (temporary connections) were labile and not predictably persistent.

A new approach by John *et al.* (*2*), in which an analysis of correlation coefficients for changes in evoked-potential configurations was made during conditioning, holds promise of producing important data on brain function and "learning." Whether changes in the wave forms of evoked potentials associated with temporary connections in John's experiments are consistent and persistent remains to be demonstrated. Our experiments on brain stimulation and conditioning indicate that some neural changes associated with conditioning may be remarkably stable and persistent (*3*).

The interhemispheric delayed response (IDR) represents neural activity in a labile, multisynaptic system linking the cerebal cortex of both hemispheres by way of the brain stem (*4, 5*). In the cat, locally anesthetized, anesthetized with chloralose, or unanesthetized and carrying implanted brain-electrodes, the IDR can be recorded from the surface of the anterior middle suprasylvian gyrus after electrical stimulation of the contralateral homotopic area. The evoked response is initially positive and, compared with the transcallosal response, has a much longer latency (40 to 65 msec).

In long-term experiments, electrical stimulation of the same suprasylvian gyrus area in the cat, by means of implanted electrodes, has been used as the conditional stimulus to elicit foot flexions (*6*). I have attempted in the present study to relate changes in the IDR to the "learned" responses elicited by chronic electrical excitation of the cerebral cortex.

Ten cats with unilaterally or bilaterally implanted electrode units over the suprasylvian gyri (Fig. 1*A*) received daily sessions of brain stimulations while loosely restrained in a conditioning apparatus. For seven of the cats, brain stimulation as the conditional stimulus was paired with foot shock as the unconditional stimulus (*6*); these animals were trained to at least a 60-percent level of conditioned responses and then overtrained to an average of 930 total pairings (range, 345 to 1250). The three control cats received 640, 1025, and 1050 brain stimulations, but without the unconditional foot shock. The seven experimental cats received an average of 50 sessions of brain stimulation (one session daily); the control cats received an average of 60 sessions.

Cortical potentials evoked by auditory clicks, photic flashes, and by contralateral cortical electrical stimulation were finally studied in terminal experiments with all ten cats; standard stimulating and recording procedures (*5*) were used, with the animals under general anesthesia. For three of the experimental cats additional recording sessions were completed before the chronic brain stimulation and again before the terminal experiment; the implanted electrodes were used for stimulating and for recording. No differences in evoked potentials between the hemispheres were observed in the three cats in the initial control experiments.

Recordings of electrical responses, in

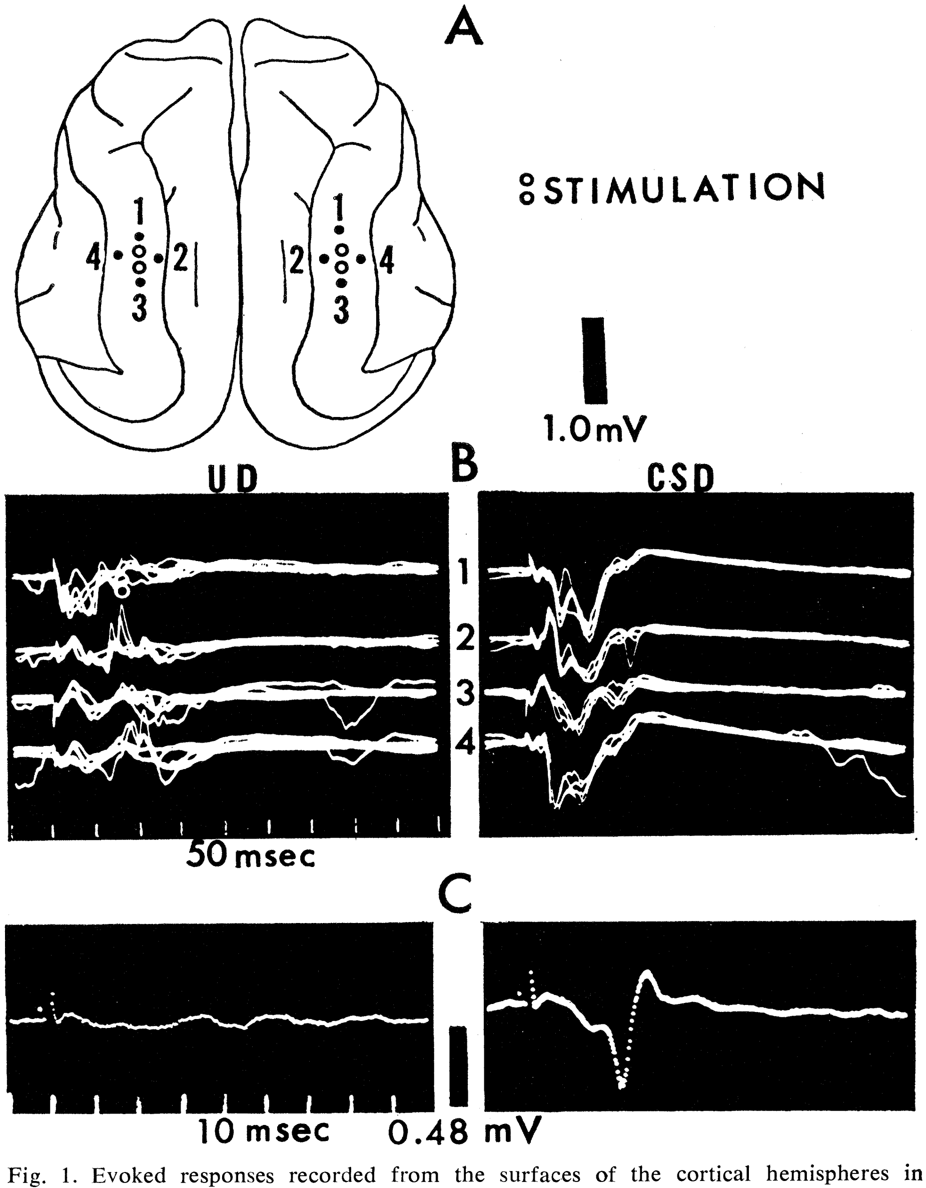

Fig. 1. Evoked responses recorded from the surfaces of the cortical hemispheres in terminal experiments on two trained cats (*B* and *C*). Responses were elicited by contralateral cortical stimulation. Chloralose anesthesia. Positive deflection is down, here and in Fig. 2. *A*, Location of permanently implanted electrodes (open circles) and of the recording points used in the terminal experiment (filled circles). *B*, Responses from an animal that had received chronic stimulation consisting of 1000 pairs of left-cortex and foot shocks over 54 days; a 70-percent level of conditioned response was reached after 215 pairings. CSD responses (right) contralateral to the chronically stimulated cortex. UD responses (left) from the chronically stimulated side to contralateral stimulation. Chronic stimulation: 2-second trains of 1-msec pulses at 50 per second and 0.45 ma. Acute stimulation: 1 per 3 seconds; pulse duration, 0.1 msec; 9.9 volts (about 0.9 ma). Superimposed sweeps. *C*, Records from Mnemotron computer of average transients (50 sweeps), obtained from the cortex at the sites of permanently implanted electrodes. Responses were elicited by contralateral cortical stimulation. CSD and UD interpreted as in *B*. Chronic stimulation was to the left side for 58 days; 910 pairs, 460-percent overtraining. Chronic stimulus parameters as in *B*, but at 0.6 ma. Acute stimulation: 1 per 3 seconds; pulse duration, 0.2 msec; 3.2 volts (about 0.3 ma).

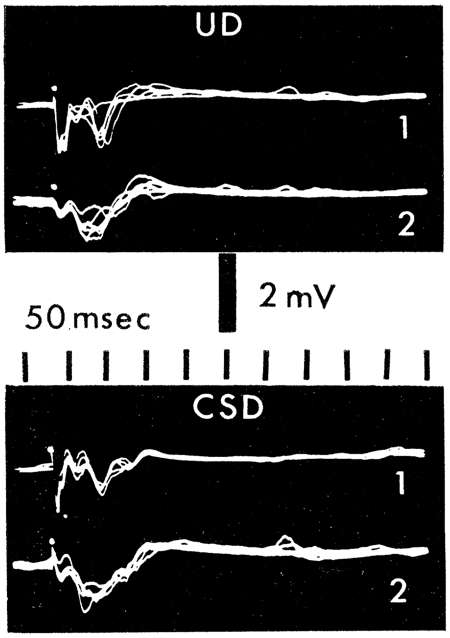

Fig. 2. Evoked responses as in Fig. 1, but in a control animal. Recording sites approximately those of the permanently implanted electrodes. CSD and UD interpreted as in Fig. 1. Chronic brain stimulation was to left suprasylvian gyrus, not paired with foot shock, 1025 times over 69 days. Chronic stimulation as in Fig. 1*C*. Acute stimulation as in Fig. 1*C*, but at 9 volts (about 0.9 ma). Superimposed sweeps.

all animals, were identified as CSD (in the "chronically stimulated direction") or as UD (in the "unstimulated direction"). The CSD responses were evoked by electrical stimulation of the cortical area that had received the chronic electrical stimulation and by peripheral stimuli. The CSD responses were recorded from the surface of the cerebral cortex contralateral to the side that had received the chronic stimulation. The UD responses were evoked by electrical stimulation of the cortex on the side contralateral to that which had received the chronic stimulation, and by peripheral stimulation. The UD responses were recorded from the cortex on the side that had received the chronic stimulation.

Figure 1 shows evoked IDR's recorded from two cats in terminal experiments. In *B* the IDR occurs at all four points (CSD, right) as a single or double positive deflection peaking at 30 to 55 msec; maximum amplitude is 800 μv. The UD responses (left) show an IDR with a much lower amplitude—only about 300 μv. Transcallosal responses are about equal on both sides.

In *C*, for the second cat, a large-amplitude IDR is present (CSD), while no IDR was observed on the chronically stimulated side (UD). The IDR amplitudes, for all seven cats in these experiments, were always greater for CSD. Differences between CSD and UD amplitudes ranged from 80 to 750 μv, with an average of 400 μv. Not only were IDR amplitudes increased, but IDR thresholds were much lower in the "chronically stimulated direction."

These findings of enhancement of the IDR in the "chronically stimulated direction" in the seven cats contrast with the data from the three cats which had received chronic brain stimulation but no foot-shock pairings. At the two cortical locations, left and right suprasylvian gyri, the IDR's were of similar amplitude. One set of records is shown in Fig. 2.

In the one cat tested, the enhanced IDR was persistent. This animal, after 420-percent overtraining, was put aside and received no further training or brain stimulation for 3 weeks prior to the terminal experiment. During this experiment, by the use of computer averaging, a 300 μv IDR was recorded in the "chronically stimulated direction," whereas no IDR could be recorded in the "unstimulated direction" even when 50-percent higher stimulus was used.

It may be argued that the chronic electrical stimulation could produce some unspecific "sensitization" of cortical tissue, which would result in altered evoked responses. No such changes were apparent. In most animals there were no consistent differences, between the chronically stimulated and unstimulated suprasylvian gyri, in potentials evoked to peripheral photic or auditory stimuli. There was likewise no difference in transcallosal response between the two sides.

These experiments seem to demonstrate that facilitation in a multisynaptic pathway can be accomplished by prolonged pairing of direct electrical stimulation of the pathway with a foot shock in a conditioning situation. The IDR enhancement is only in the direction of the chronically stimulated side to the contralateral cortex. Brain stimulation alone, without the reinforcing foot shock, produces no evidence of enhanced conduction in the IDR pathway in either direction.

It has been established by Morrell (*7*) and others that persistent changes in spontaneous activity and in the direct cortical response are observed following continuous epileptiform bombardment from the opposite hemisphere. Similar electrical changes have not, as yet, been related to behavior, and thus no ready comparison with the present experiments is possible.

The enhanced IDR may be more persistent than the electrical changes in evoked potentials and the EEG associated with "learning," as reported by others. Whether any structural changes may be related to the observed evidence for functional changes must await a careful histological study of the cortical and subcortical elements involved.

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Retrograde Amnesia from Electroconvulsive Shock in a One-Trial Appetitive Learning Task

Abstract. *Rats deprived of water were placed, for 4-minute sessions, into a chamber containing a hole in one wall. After several sessions the number of times these rats explored the hole markedly decreased. Rats given access to water at the hole for a brief period explored the hole more frequently than controls, when they were tested later. This increase in hole explorations was abolished when the water reinforcement was followed by electroconvulsive shock but not when followed by foot shock.*

One-trial conditioning techniques are useful and at times essential in studying retrograde amnesia and the consolidation hypothesis. In all of these