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CHANGES IN VISUAL RECOVERY FUNCTIONS AND UNIT ACTIVITY PRODUCED BY FRONTAL AND TEMPORAL CORTEX STIMULATION[1]

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Previous reports (Dewson *et al.* 1966; Spinelli and Pribram 1966) described the effects of chronic electrical stimulation and of ablations of the posterior sensory-specific "association" cortex on the recovery of responses evoked by paired flashes and clicks in the primary projection systems. These experiments demonstrated the corticofugal control which the brain can exert over its own input and provided an explanatory mechanism for the effects on behavior of lesions of the posterior "association" cortex.

The success of these studies prompted the question whether the same techniques would prove fruitful in analyzing the functions of the frontal "association" cortex. There had been some indication from neurobehavioral experiments that in certain situations the posterior and frontal systems act in opposition to one another (Pribram 1966). Would, therefore, chronic electrical stimulation of the frontal cortex produce an effect on recovery function opposite to that obtained when the posterior cortex is stimulated?

A second question raised by the initial studies concerns the validity of the interpretations based upon them. Recordings were obtained with macro-electrodes and inferences were made about an effect on populations of cells whose activities these electrodes were presumably monitoring. More direct evidence of cortical control over neural units in the input systems would be obtained if micro-electrode recordings were made.

Finally, the initial stimulation studies concentrated on changes produced in the visual cortex. On the basis of the results obtained in the auditory system (Dewson *et al.* 1966; Nobel and Dewson 1966) the cortical changes which were obtained most likely reflected the effects of stimulation on subcortical stations. This possibility needed checking.

The present report deals therefore with 3 sets of experiments: (1) the effect of chronic stimulation of frontal eugranular cortex on recovery of responses evoked by paired flashes in the visual cortex; (2) the effect of such stimulation and that of the posterior "association" cortex on flash-evoked unit activity in the visual cortex, in the lateral geniculate nucleus and in the optic tract; (3) mapping of visual receptive fields of units in the lateral geniculate nucleus.

METHOD

Experiment I

Eight rhesus monkeys were fitted with a battery powered transistorized stimulator which has, on an earlier occasion, been described in detail (Spinelli and Pribram 1966). The parameters of stimulation used in the current experiments were: 9/sec, 1 msec duration, 2.5 V amplitude. While the monkeys were unanesthetized, completely awake and sitting in a restraining chair, recordings were made from 300 μ nicrome wire bipolar electrodes, with an inter-electrode distance of approximately 3 mm, which had been implanted in their parietal, temporal, and occipital cortices. Pairs of flashes were presented at the rate of 1/sec. Fifty consecutive responses were recorded on magnetic tape and, for anal-

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ysis, accumulated on a Computer for Average Transients (CAT).

From the data, recovery functions were computed, each point on the function indicating the ratio (expressed as percent) between the second and the first major deflection recorded.

Experimental monkeys received continuous stimulation in the anterior frontal cortex; control subjects were given continuous stimulation in the parietal regions.

Experiments 2 and 3

In Experiment 2, thirteen cats and in Experiment 3, ten cats were used. The surgical procedures and general recording techniques were the same for both experiments.

Surgical procedures. All cats were anesthetized with thiopental sodium injected i.v. Atropine sulfate (0.4 mg/kg) was given i.p. before surgery. A polyethylene tube was inserted in the radial vein for administration of saline, glucose, and gallamine triethiodide (Flaxedil). Homatropine, Dorsacaine, phenylephrine, were instilled in the eye (Spinelli *et al.* 1965) and contact lenses were used to protect the eye and correct for accommodation. A tracheal cannula was inserted to allow artificial respiration. All incisions and pressure points were infiltrated with a long acting solution in oil of procaine (Zyljectin).

A small trephine hole was made in the skull, the dura opened and the exposed cortex covered with a solution of agar in saline to minimize brain pulsation. Great care was taken in the experiment to avoid pain to the animal and the cat's rectal temperature was maintained throughout the experiment at 38° ± 0.5° C with a heating pad (Spinelli *et al.* 1965).

Flash stimulation and recording techniques. Flashes of light, delivered by a Grass PS-2D photostimulator set at the minimum intensity and with the flashing bulb placed at about 1 m in front of the subject were presented every 2 sec; a train of 40 10-V shocks, 1 msec in duration, and with a frequency of 100/sec was used to stimulate frontal and inferotemporal cortex before giving the flash.

An array of 4 tungsten micro-electrodes (Hubel 1957) was lowered stereotaxically and the tips aimed at the intracranial end of the optic foramen. The impedance of the electrodes used ranged from 3 to 10 MΩ and was measured with a rectangular 0.5 msec pulse.

After amplification, unit activity was photographed from an RM 564 Tektronix oscilloscope. A Schmitt trigger, which could be adjusted so as to be set off by units of amplitude above the noise level, was also used. Pulses from the Schmitt trigger were then fed to the input of a Mnemotron CAT 400A to compute post-stimulus time histograms, or to a PDP-8 computer when mapping receptive fields.

Mapping technique. Visual receptive fields of lateral geniculate cells were first located by moving a small light in front of the cat's eyes. The servo-mechanisms of an X–Y plotter were then used to move a 0.2° white disc (200 cd-m^2) on a black (0.02 cd-m^2) background in a scanning pattern, which was controlled by a small general purpose computer (PDP-8) and covered a 25° × 25° region of the visual space. This was achieved by having the computer generate appropriate electrical functions for the X–Y servo-amplifiers so that the disc would be moved on fifty 25° horizontal scans spaced 0.5° vertically. Angular displacement was set at 5° per sec, so that each horizontal scan required 5 sec; 1.5 sec were allowed before the next scan. The spikes generated by the cell during 0.5° segments were counted and stored separately by the computer. Fifty data points were therefore collected during each scan and a matrix of 50 × 50 data points for the whole mapping procedure. The computer could then be asked to display on an oscilloscope face only those points where activity had exceeded the mean background. This method has been described elsewhere in more detail (Spinelli 1966).

RESULTS

1. *The effect of chronic stimulation of frontal cortex on recovery functions evoked by paired flashes in the visual cortex*

The hypothesis that frontal stimulation would speed recovery was confirmed as shown in Fig. 1. Note, however, that the results of frontal lobe stimulation do not form an exact mirror image of those obtained when the inferior temporal cortex is stimulated; there is considerably greater fluctuation in the "frontal" curve.

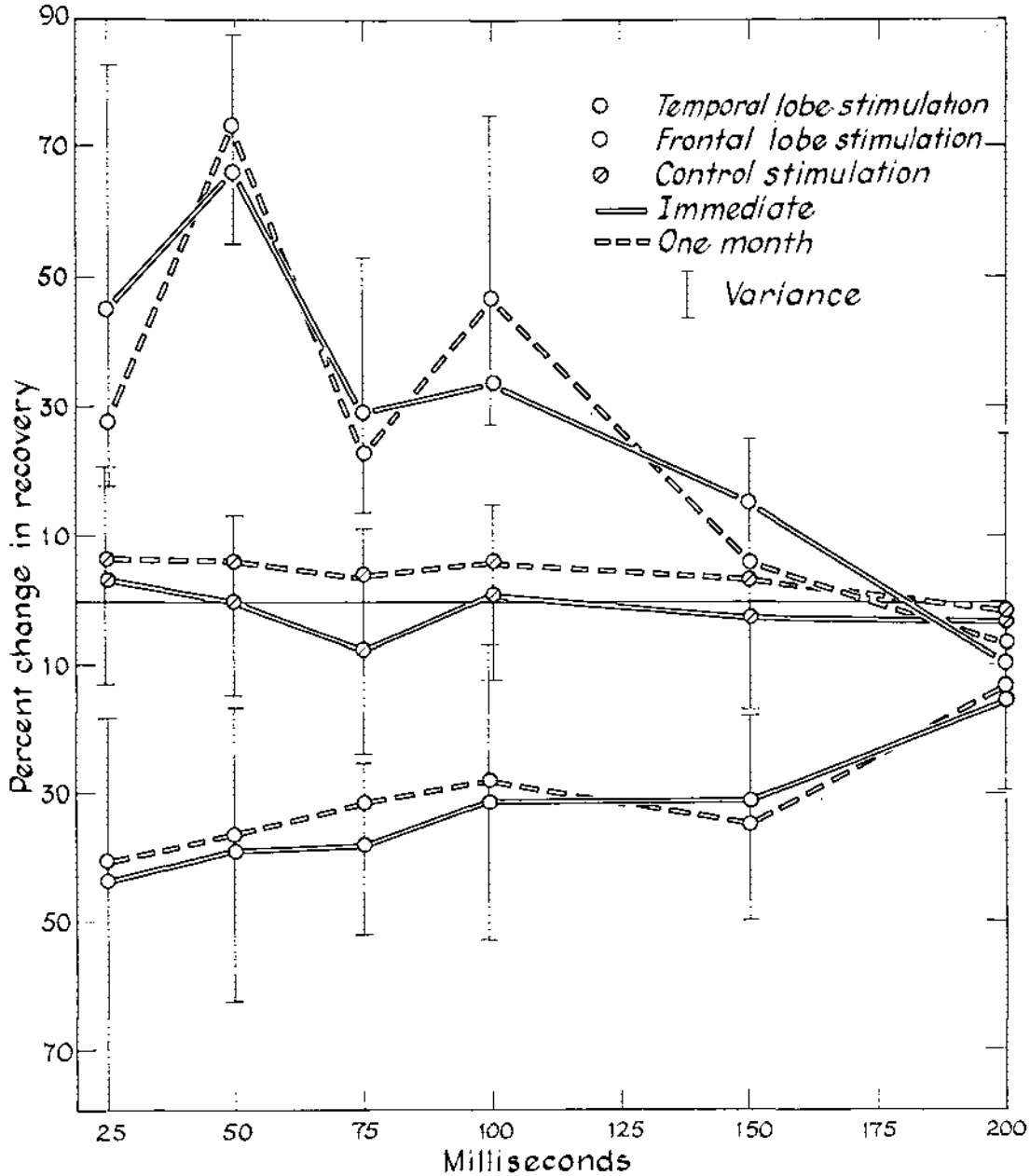

Fig. 1

The change in recovery of a response to the second of a pair of flashes compared with the pre-stimulation recovery function. Control stimulations were performed on the parietal cortex. Records were made immediately after the onset of stimulation and weekly for several months. The response curves obtained immediately after onset and after 1 month are presented. Vertical bars represent variability of the records obtained in each group of four monkeys.

This result led us to analyze the variability which occurs in the initial one of the flash-evoked pair of responses. An analysis of variance showed the initial responses of the frontally stimulated group of monkeys to vary more than those of the combined temporal and control groups ($F = 3.794$, $P < 0.02$). These results were obtained from the Computer for Average

Transients' (CAT) summated records which are designed to eliminate variability: it is likely therefore that the actual difference in variability of the raw scores would be even larger.

2. *The effect of electrical stimulation of the frontal and inferotemporal cortex on flash-evoked unit activity in the visual cortex, lateral geniculate nucleus and optic tract*

For these experiments Flaxedilized cats were used and units in the posterior part of the marginal gyrus were studied. Electrical stimulations were made in the gyrus proreus and the hippocampal fusiform gyrus. The cortex of this latter gyrus was thought to be homologous with the inferotemporal cortex of monkey on the basis of experimental results reported by Blake (1964). A total of 41 such units were examined. These could be classified into 2 groups: (1) 11 "off" units which responded to the flash by a marked diminution of their "spontaneous" rate of firing, and (2) 30 "on-off" units which responded by a burst of increased activity followed by a marked diminution of activity below base line. Cortical stimulation failed to affect 7 (or 17%) of these units. The others showed some change in the duration of the "off" period. The changes obtained are summarized in Table I.

These results would suggest that frontal stimulation tends to lengthen the off period of "off" units and to shorten this period in "on-off" cells, whereas stimulation of the inferotemporal cortex tends to produce the opposite effect. This "opposite" effect was most clearly observed in units which were held for a sufficient time to allow both frontal and temporal lobe stimulation to be made.

In the lateral geniculate nucleus 14 units were examined. Of these, 4 failed to be influenced by either frontal or temporal lobe stimulation and 5 were influenced by both. Altogether, the firing pattern of 8 units was altered by frontal lobe stimulation and that of 7 units by inferotemporal cortex stimulation.

The configuration of the change produced in the firing cells in the lateral geniculate nucleus was essentially similar to, but more consistent than that produced in the cortex: all geniculate cells examined were "on-off" in type and frontal lobe stimulation shortened their off period while inferotemporal stimulation lengthened it.

In the optic nerve 16 units were examined and all but 2 of these showed some change in firing pattern when frontal or inferotemporal stimulation was added. Seven units were influenced by both. Altogether, 11 units were influenced by frontal and 10 units by inferotemporal stimulation.

The configuration of the change produced in the firing of cells in the optic nerve differed considerably from that obtained in the geniculate and cortical stations. At the optic nerve location, both frontal and temporal lobe stimulation produced effects in the same direction though these varied from unit to unit: usually a more even distribution of firing resulted, although in 3 units a sharpening of the "on" peak and lengthening of the "off" period resulted from frontal stimulation. In general, however, more activity appeared in the "off" period and the peak of the "on" period became flatter and broader. The opposing effects of frontal and temporal cortex stimulation were not observed at the optic nerve level.

TABLE I

Classification of units in the primary visual cortex and the effect on the "off" period of temporal and frontal stimulation

	Stimulation	Off period	No. of units	Percent units
"Off" units (9)	Frontal	Lengthened	8	100
	Temporal	Shortened	1	
"On-off" units (25)	Frontal	Lengthened	4	22
	Frontal	Shortened	14	78
	Temporal	Lengthened	7	100
	Temporal	Shortened	0	0

3. *The effect of electrical stimulation of the frontal and inferotemporal cortex on visual receptive fields of units in the lateral geniculate nucleus*

The experiments on lateral geniculate units will be reported here only briefly as they are to form the subject of a separate paper. Changes in the configuration of visual receptive fields were clearly produced in 27 of 50 units examined in the lateral geniculate nucleus by frontal and inferotemporal stimulation. Fig. 2 shows a unit which becomes more active during frontal and less active during inferotemporal stimulation. Often, the changes produced by frontal and temporal lobe stimulation, though differing from one another, are difficult to classify. In general, however, stimulation of the inferotemporal cortex tends to act in the opposite direction of frontal cortex stimulation. Changes in the level of facilitation or inhibition of a unit have the effect of bringing out or of fading some features of the receptive field.

DISCUSSION

The results obtained in these experiments confirm and extend those previously reported (Dewson *et al.* 1966; Spinelli and Pribram 1966). Frontal as well as temporal lobe stimulation influences the recovery of responses to pairs of flashes recorded from the visual cortex of awake monkeys.

In addition, frontal lobe stimulation increases the variability of the initial responses to the pair of flashes.

Further, electrical stimulation of these cortical "association" areas influences the flash-induced firing pattern of units in the primary visual system, not only in the cortex but also in the lateral geniculate nucleus and in the optic nerve.

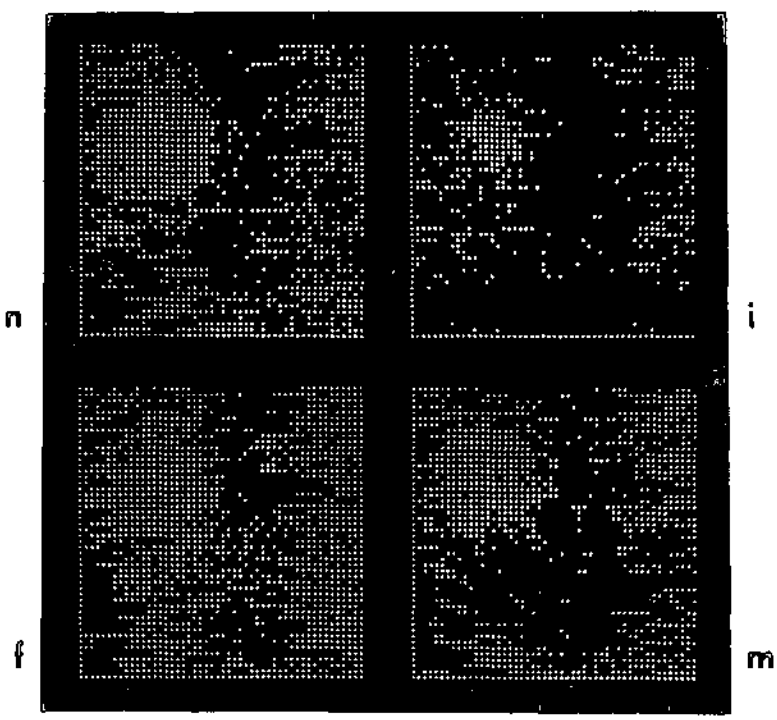

Fig. 2

Receptive field maps from a lateral geniculate unit. n, top left: control; i: mapped while inferotemporal cortex was being stimulated; f: mapped during frontal cortex stimulation; m, bottom right: final control. A third control was taken between the i and the f maps and was not included because it was not significantly different from the first and the last. Note that inferotemporal stimulation decreases the size of the "on" center; frontal cortex stimulation, while not really changing the circular part of the receptive field, brings out another region below it. The level of activity shown is 3 standard deviations above the normal background for this unit.

In the visual cortex and lateral geniculate nucleus, the pattern of change produced by the frontal cortex stimulation is, in general, in a direction opposite to that obtained when the inferotemporal cortex is stimulated. In the optic nerve, the effects of stimulation of the 2 cortical areas appear to parallel one another.

There can thus be no question that electrical stimulation of the frontal "association" cortex, as well as of the inferotemporal cortex, influences the activity evoked by flashes in the visual system. As already noted, at the cortical and geniculate levels the influence of frontal stimulation is opposite to that produced by temporal cortex stimulation. In addition, an increase in the variability of the response of the system is also produced.

These electrophysiological results may be usefully juxtaposed to those derived from neurobehavioral studies. Ablation of the anterior frontal cortex (which probably produces an effect opposite to that resulting from stimulations such as those reported here—Dewson *et al.* 1966) leaves monkeys unable to perform tasks which vary from trial to trial (Nissen *et al.* 1936; Pribram 1961). Analysis of this disability has led to the suggestion that the difficulty reflects a greater susceptibility to pro- and retro-active interference; *i.e.*, that for frontally lesioned primates each trial tends to interfere with the next, and is interfered with by its predecessor (Malmo 1942; Meyer and Meyer 1966). The suggestion is that the frontal lesion interferes with temporal resolution. Although the time course and situation are considerably different, the results of the experiments reported here suggest that frontal stimulation improves temporal resolution in the input channels. The results of the 2 types of studies are thus in consonance.

The micro-electrode studies validate the conclusion based on the macro-electrode data, that electrical stimulations of the "association" areas of the cortex influence the activities of the primary projection systems, both at the cortical level and at subcortical stations. Here again, the effects of temporal and frontal lobe stimulation tended to produce opposite results—though not as uniformly as when macro-electrodes were used. Also, at the optic nerve such "opposition" was *not* found. Observations of the effect of such stimulation on geniculate unit receptive fields suggest that inferotemporal and frontal lobe stimulation tend to alter the configuration of the field through inhibitory and excitatory mechanisms respectively.

SUMMARY

Chronic electrical stimulation of the frontal cortex of awake monkeys enhanced the recovery functions recorded from electrodes implanted in the striate cortex. The effect is opposite to that obtained when the inferotemporal cortex is stimulated in this fashion. Further, unit activity at cortical and geniculate stations (recorded from cats) was, as a rule, reciprocally influenced by frontal and temporal cortex stimulation. Such a reciprocal effect was not obtained at the optic nerve level where the effects of the cortical stimulation, though marked, were indistinguishable from one another. Observations of the effect of such stimulations on unit activity in the lateral geniculate nucleus suggest that inferotemporal cortex excitation alters the configuration of the receptive field while frontal cortex stimulation influences the background activity of the unit.

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