

CHANGES IN VISUAL RECOVERY FUNCTIONS PRODUCED BY TEMPORAL LOBE STIMULATION IN MONKEYS¹

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INTRODUCTION

Agnosia, an inability to identify objects due to brain injury, is a clinical syndrome of central interest to an understanding of cognitive processes. To advance this interest, an attempt was made to produce the syndrome in animals and this attempt proved successful: monkeys with partial ablations of the posterior "association" cortex have been shown impaired either in visual (Blum *et al.* 1950; Chow 1952; Mishkin and Pribram 1954), somesthetic (Pribram and Barry 1956; Wilson 1957), auditory (Mishkin and Weiskrantz 1958), or gustatory (Bagshaw and Pribram 1953) discriminations depending on the locus of the lesion. In each case, it was established by the technique of the intersect of sums of lesions and effects (Pribram 1954) that the effect of the lesion was modality specific; *i.e.*, the ablation which disrupted visual behavior had no effect on somesthetic, auditory, and taste discrimination; the ablation which disrupted somesthetic behavior had no effect on visual behavior, etc. Thus the so-called "association" cortex of monkey turned out to be divisible into areas, each of which served one or another specific sensory mode².

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² The so-called association cortex of man and monkey which is referred to here is that part of the cortex which is "silent" when electrical responses are evoked elsewhere by peripheral stimulation. For this reason and others, the primate "association" areas are thought to be different from the "association" cortices recently described for the cat in the electrophysiological literature. These latter electrophysiologically-determined areas appear to be true multisensory afferent association systems. The primate cortex referred to here might better be called "intrinsic" (see Pribram 1960) or "associated" areas but for convenience will continue to be labeled "association", the

These impairments were analyzed further and were shown to involve both an apparent loss of acuity (Mishkin and Hall 1955; Pasik *et al.* 1958a, b) and a difficulty in making the appropriate response to readily discriminable cues (Pribram and Mishkin 1955; Ettlinger 1959a). The suggestion was therefore made that the difficulty was manifested in searching and selecting, both among alternative cues (Pribram 1960) and among the distinctive features of a single cue (Butter *et al.* 1965; Butter, *in preparation*). Experimental results have amply confirmed the hypotheses derived from this suggestion.

The dilemma posed by these neurobehavioral data can be stated briefly. Anatomically, the lesions which produce the effects are limited to association cortex; *i.e.*, they remain clear of the classical projection areas. This is ascertained by the fact that retrograde degeneration in the primary projection nuclei of the thalamus does not occur. Yet the effects of ablation are sensory mode specific. The question thus arises how this modality-specific function is effected. The attempt to attribute the specificity to a restricted input from one or another sensory system meets with difficulties which are as yet not resolved. Lesions of input fibers, whether at the thalamic or cortico-cortical level, fail as a rule to disrupt discrimination. The one exception is the total isolation of the "association" cortex from ipsi- and contralateral input by ipsilateral sensory nerve section or sensory cortex resection and additional severance of the corpus callosum (Mishkin 1958; Ettlinger 1959b).

An alternative and complementary approach to the dilemma of sensory mode specificity of the association areas is that they exert their influence

quotation marks indicating the apparent impropriety of this appellation.

via a corticofugal, efferent pathway which alters the functional activity of the primary sensory system (Pribram 1958). According to this approach, the effects of the removal or of the stimulation of the visual association cortex, for instance, would be selectively discernible in the primary visual system; the removal or stimulation of the auditory association cortex would be selectively discernible in the primary auditory system, etc. The purpose of the experiments reported here was to take some initial steps to test whether indeed such efferent control by "association" cortex over primary projection systems can be demonstrated. Specifically, in fully awake monkeys uninterrupted, continuous electrical stimulation was applied via electrodes bilaterally implanted in the visual association area which lies on the inferior surface of the temporal lobe. The effects of such stimulation were assayed by recording responses to flash and to click from other arrays of electrodes implanted in the primary visual and in the primary auditory cortical areas. The effects of the inferotemporal stimulation were compared with those from stimulations of other cortical areas, and with the responses obtained in the pre-stimulated condition. Finally, we tested the effect of continuous stimulation on the learning of two discrimination tasks.

METHOD

A transistorized stimulation device was implanted in 5 rhesus monkeys. This consisted of a transistorized blocking oscillator powered by 2 nickel-cadmium rechargeable batteries. Leads from the plus and the minus of the batteries are connected to a plug that is secured with dental cement to the skull of the animal. Through these leads the batteries can be recharged when needed. To the plug are also connected the output of the stimulator, the center tap of the transformer and the electrodes implanted in the structures to be stimulated. The stimulator itself is buried in the cement and delivers bipolar pulses of 1 msec duration, 2.5 V amplitude, the frequency of the pulses being determined by R_1 (10 p/sec when R_1 is 120,000 Ω) and is activated by connecting the minus of the battery with the center tap of the transformer. This is done externally with a male plug which also connects the output of the stimu-

lator with the appropriate stimulating electrodes. The life of the batteries depends on the desired frequency and it is of the order of 10 weeks for a frequency rate of 1/sec.

The stimulus parameters used in the experiments were: 9/sec, 1 msec duration, 2.5 V amplitude. In addition, 300 μ microme wire bipolar electrodes with an interelectrode distance of approximately 3 mm were implanted in the parietal, temporal, and occipital cortices of these animals.

Recordings were made in unanesthetized, completely awake monkeys sitting in a restraining chair. Pairs of flashes, of clicks and of click-flashes and flash-clicks were presented at the rate of 1/sec. Fifty consecutive responses were recorded on magnetic tape and, for analysis, accumulated on a Computer for Average Transients (CAT).

Polaroid photographs were made from a slave scope which was ganged to the output of the computer. From these photographs recovery functions were computed, each point on the function indicating the ratio (expressed as percent) between the second and the first response evoked by the pair of flashes. Measurements were made on the first major deflection recorded.

Experimental monkeys received continuous stimulation in the inferior temporal cortex; control subjects were given continuous stimulation in the parietal and precentral regions.

In addition, 3 monkeys were tested in a simple and in a more complex visual discrimination situation. The apparatus used was a special purpose computer (DADTA) (Pribram *et al.* 1962) designed to randomize over 16 possible positions the cues to be discriminated. Rewards (peanuts) were delivered according to a preset program whenever the correct choice was made by the monkey. Each choice was recorded on tape for easy general purpose computer processing. Each monkey was allowed 50 choices per day until he solved the discrimination problem. Solution of the problem consisted of a performance level of 90% on 100 consecutive choices; *i.e.*, two days.

The first problem consisted of a choice between the numerals 3 and 8. The second required discrimination of the letter M from the set of letters M K H N A.

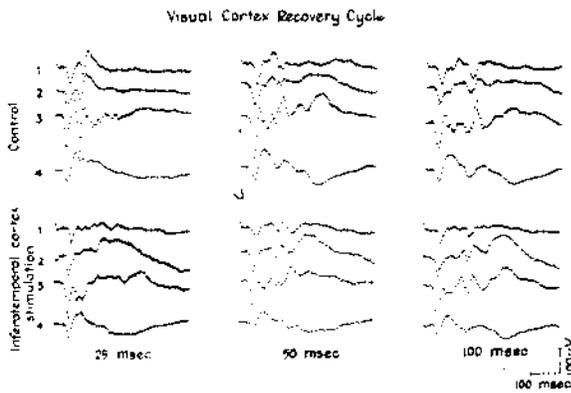


Fig. 1

A representative record of the change produced in visual evoked responses by chronic stimulation of the inferotemporal cortex. Upper set of records was taken before stimulation; lower set, during stimulation. All traces were recorded from the visual cortex; the first set in response to a single flash, the second to pairs of flashes separated by 75 msec and the third to pairs of flashes separated by 150 msec. Note here the change in recovery phenomenon and in wave form of the response even with a single flash. However, this was not a constant finding.

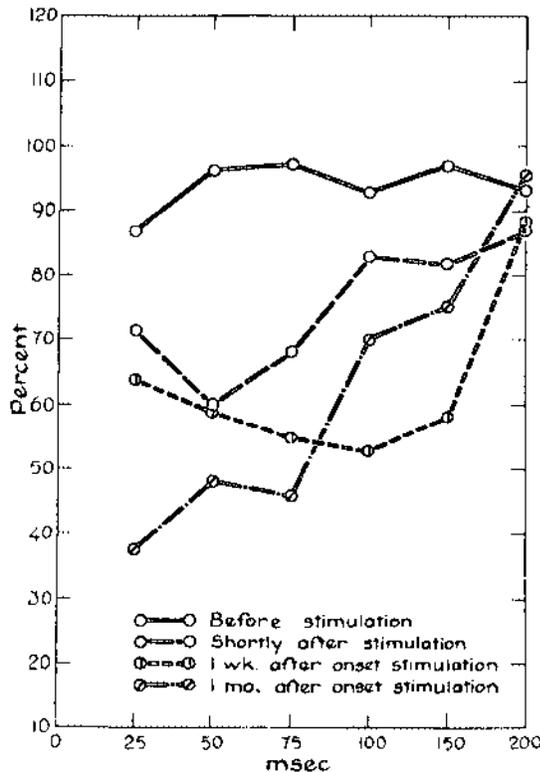


Fig. 2

A plot of the recovery functions obtained in one monkey before and during chronic stimulation of the inferotemporal (I.T.) cortex.

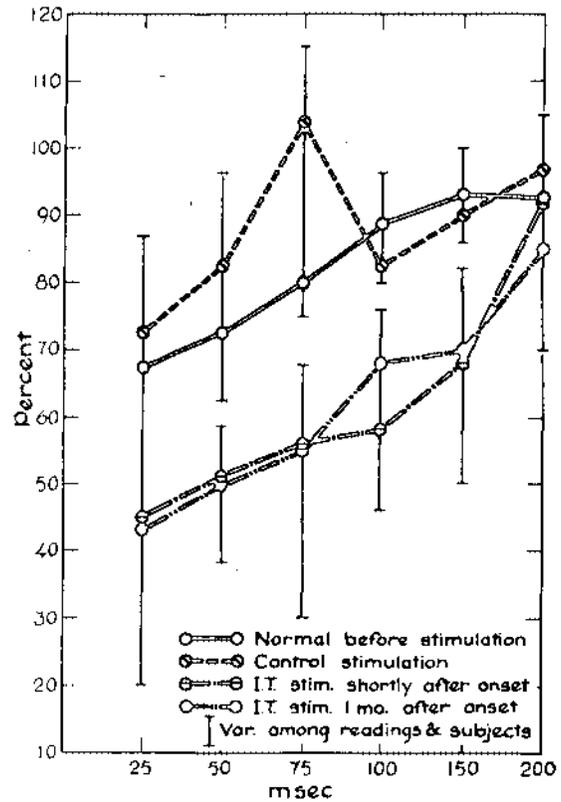


Fig. 3

A plot of the recovery functions obtained in 5 monkeys before and during chronic cortical stimulation. See text for details.

RESULTS

The results are portrayed in a representative record (Fig. 1) and in plots of recovery function (Fig. 2 and 3). Fig. 2 shows the change in recovery of visual system of one monkey when pairs of flashes are presented and the inferotemporal cortex is stimulated. Each point on the graph represents the average of 4 electrode placements and therefore of 200 evoked responses. Fig. 3 shows the group changes obtained in the experiment. Each point on the graph of the pre-stimulation and experimental results represents the average obtained from 20 electrode placements (and therefore 1000 evoked responses) in five monkeys; each point on the graph of the control results represents the average obtained from 8 electrode placements in two monkeys and therefore 400 evoked responses. (Two of the monkeys served first as controls and subsequently as experimental subjects.) The extent of the

TABLE I
Trials to criterion taken by control monkeys and by monkeys in which
the inferotemporal cortex was stimulated

Control monkeys			Stimulated monkeys		
Subject	Trials		Subject	Trials	
	3 vs. 8	M vs. K, H, N, A		3 vs. 8	M vs. K, H, N, A
160	280	800	156	50	375
162	180	400	183	200	700
165	280	550	198	199	550
170	350	700			
Average	272	612		183	542

variability is shown by the bars perpendicular to the recovery function.

At 25 msec the spread of variability among the unstimulated *Ss* was great. For some monkeys the initial response to the second flash, superimposed on a large wave, which is continuous with the initial response evoked by the first flash, was hardly appreciable. Other monkeys, however, showed a clear and measurable separation between the responses evoked by the two flashes — and two of these monkeys showed remarkably good recovery even at this short interval. At 50 msec there was a clearly discernible second response in all *Ss* with moderate to excellent recovery. By 100 msec recovery was almost complete. Extreme variability among *Ss* at the short intervals (25 msec or less) has also been reported to be present in man (Schwartz and Shagass 1964). This intersubject variability was in marked contrast to the stability shown by any one subject (unstimulated) on successive runs, even though these were made weeks apart.

Effects of continuous inferotemporal stimulation on the click-evoked recovery functions was also studied in the same monkeys and no reliable changes were observed to take place. On the other hand, in two monkeys the click-evoked response *per se* gradually increased in amplitude over the month of chronic, continuous stimulation. A similar increase in amplitude was observed in visually evoked responses in one of these subjects and in another whose auditory response showed no such change. Click-flash and flash-click interactions did not occur nor did chronic, continuous stimulation influence this non-occurrence.

In summary, the results of this series of experiments show that recovery of responses evoked in the occipital cortex by pairs of flashes is depressed by continuous stimulation of the inferotemporal "association" cortex. This depression lasts over at least 2 months of continuous stimulation. No such effect was seen on responses evoked in the posterior part of the supratemporal plane by pairs of clicks nor did continuous stimulation of parietal cortex influence visual and auditory recovery functions.

During this period of continuous stimulation both discrimination tasks were learned with alacrity. Comparison with a control group of monkeys shows the stimulated monkeys to be normal in achieving solution on both tasks (Table I).

DISCUSSION

The results of this series of experiments demonstrate that the inferotemporal, and not other parts of the posterior "association" cortex, exerts control on the visual system. Further, this control is not effected on auditory responses.

Another series of experiments performed in our laboratory has pursued the problem of association cortex control over auditory functions (Dewson, Nobel and Pribram, in preparation). These experiments were performed in awake cats who had electrodes implanted in their cochlear nuclei. The insular-temporal area was removed in these subjects. In prior experiments (Dewson 1964) such removal had resulted in a selective inability to discriminate vowel sounds; pitch and loudness discrimination remained intact. Bilateral

al removal of insular-temporal cortex was found to speed up response recovery in the cochlear nucleus when the cat was presented with paired clicks. Thus removal of the "association" cortex produces effects opposite to those found to occur in the present experiment upon continuous stimulation.

In a subsequent experiment this cortical influence on responses in the cochlear nucleus was shown to be mediated via an efferent path synapsing in the inferior colliculus (Nobel and Dewson, in preparation). In the present experiments, therefore, the efferent control exerted by the inferotemporal cortex in monkey must not be assumed to influence directly the cells of the occipital cortex — an influence via a tract leading to some subcortical station such as the superior colliculus remains a distinct possibility to be explored experimentally.

The nature of the control on visual function is to produce a delay in the recovery function obtained when records are made of responses in the visual cortex to pairs of flashes. If one is allowed the assumption that the percent recovery obtained with gross (albeit small gross) electrodes reflects accurately the functions of the cell aggregate from which the record is made, a model can be usefully described. This model assumes that recovery functions measure the rate with which nerve cells, after being excited, again become available to stimulation. As the primary visual system is continuously functioning, a delay of recovery would mean that some of the cells remain "occupied" for a longer time and that each new stimulus thus finds fewer cells available. This would, in effect, reduce the redundancy with which the system operates. In another context Lindsley (1961) has suggested that this decoupling of the functions of cell aggregates is reflected in a desynchronization of their electrical activity and that such desynchronization is evidence of an increased complexity of operation of the system.

There are many experimental results which suggest that under normal circumstances the visual system operates with a considerable reserve redundancy in handling inputs made to it (Attneave 1954). The proposal has been made (Barlow 1961) that one of the chief functions of the central visual mechanism is to reduce

redundancy. We interpret our results to be in consonance with the hypothesis that ablation results in greater redundancy while both continuous stimulation of the inferotemporal cortex and the normal ordinary activity of this cortex facilitates redundancy reduction. This would be accomplished by the process which keeps some cells in the system "occupied" for a prolonged time with the result that iterated visual inputs find different populations of cells "receptive." Such a process would effectively desynchronize and multiplex the visual channel and thus increase complexity and "uncertainty" within the system, making the organism more attentive to alternatives.

The excellent discrimination problem-solving ability of the stimulated animals in this study and the marked deficiencies in search and sampling alternatives that follow ablation of the inferotemporal cortex support the formulation presented. According to this model then, pathology of the "association" cortex — by producing, via efferent pathways, a simplification of the structure of the sensory processing channel — would result in agnosia.

SUMMARY

The effect of continuous stimulation of the inferotemporal portion of the posterior "association" cortex on potential changes evoked in a primary sensory projection area was studied and changes were found to occur. Further, these changes were found to be restricted to one sensory mode. Lastly, the changes were of such a nature that they permit a model of the action of this system to be suggested.

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