The effects of inferior temporal and dorsolateral frontal lesions on serial-order behavior and visual imagery in monkeys

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Four monkeys were trained preoperatively on a serial-order task to respond to a set of five visual stimuli in a fixed sequence independent of their location. They were then given a test of visual imagery in which only two of the five stimuli appeared at a time, and the animals were required to respond to them in the order in which they appeared in the original sequence. The monkeys then received bilateral lesions of either inferior temporal cortex or dorsolateral frontal cortex. Dorsolateral frontal lesions had no effect on either serial-order behavior or visual imagery. In contrast, inferior temporal lesions severely impaired serial-order behavior. Once the serial-order task was relearned, however, the inferior temporal animals were completely normal on the test of visual imagery.

INTRODUCTION

Although the scientific study of visual imagery has a long history 20, the study of the neural basis of visual imagery is relatively new. A central question is whether visual imagery, or 'seeing with the mind's eye', taps the same neural representations as those used in visual perception. Although opponents of this view exist 19,26,29, converging evidence from different areas of neuropsychology indicates that similar neural mechanisms underlie visual imagery and perception (for reviews see refs. 6–8 and 20). In particular, event-related potential studies 5,10, regional cerebral blood flow studies 13–15, as well as studies of patients with brain lesions 11 all support the view that cortical visual areas are active during visual imagery.

One shortcoming of these studies, as noted by Farah 5, is that the techniques used with humans are often too crude to distinguish the contributions to visual imagery made by the different visual cortical areas. Thus although activation occurs in striate and some extrastriate visual areas during visual imagery tasks in humans, it is unclear at present which activation is crucial to the imagery process. The monkey provides a means to help distinguish between these possibilities since its visual areas are both well mapped and well suited to selective lesions.

The purpose of this study was to examine the consequences of bilateral inferior temporal (area TE 34) lesions on visual imagery in monkeys. Inferior temporal cortex is the final stage of cortical visual processing in monkeys 4, and damage to this area impairs visual pattern perception while leaving basic visual-sensory capacities intact 16,17. Since visual image generation requires retrieval of stored representations 8,20, we anticipated that damage to the inferior temporal cortex of monkeys, which has been implicated in both visual representation storage 33 and retrieval processes 30,31, would impair visual imagery.

The test of visual imagery employed was based on a serial-order task originally developed for use with pigeons 33 and adapted for use with monkeys 3. In the latter study, monkeys were trained to press five simultaneously presented stimuli in the order A → B → C → D → E. Reward was delivered only following a correct press to the last item of the series. Any deviation from the assigned order (for example, A → C or A → B → C → A) resulted in termination of the trial and punish-

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ment. Although from trial to trial the spatial position of the stimuli varied, the order in which they were to be pressed remained constant. Once the monkeys learned the ABCDE series, they were given a test in which all possible pairwise combinations of the stimuli (AB, AC, AD, AE, BC, BD, BE, CD, CE, and DE) were presented. The monkeys performed at high levels on the pairwise test, responding to the stimuli in the order in which they appeared in the series.

The inference that visual imagery was required to solve this pairwise test was based on two aspects of each animal’s latency data. First, the latency to press the first item of a pair increased as a function of the position of that item in the series. Second, the latency to press the second item of a pair increased as a function of the number of missing items between the first and second stimuli. These results suggested that the monkeys had formed a linear representation of the five items, and that they accessed the sequence beginning with the first item. A similar linear representational mechanism has been postulated to guide judgements of serial-order behavior in humans.

Furthermore, the orderly latency relationships observed during performance of the pairwise test are similar to the latencies observed in situations which require visual imagery in humans.

Given that inferior temporal lesions are known to impair visual discriminative behavior in monkeys, we predicted that following inferior temporal lesions the monkeys would be impaired on the serial-order task, but with retraining would relearn the task. To the extent that inferior temporal cortex is critical for retrieval processes, however, we predicted that the monkeys would not be able to perform the pairwise test, or if they were able to perform the pairwise test, then we expected that the first-item and missing-item latency effects should disappear, indicating that the monkeys were solving the task by means other than visual imagery. Two other monkeys received lesions of the dorsolateral frontal cortex.

MATERIALS AND METHODS

Subjects

Four experimentally naive male macaque monkeys (three Macaca fascicularis, one Macaca mulatta), weighing between 3.0 and 5.5 kg at the start of the study, served as subjects. The monkeys were housed individually and maintained on a diet of Purina Monkey Chow and fresh fruit adjusted to an amount that supported reliable performance.

Apparatus

All testing was conducted in a Lehigh Valley monkey chamber situated within a sound-attenuating box. The front panel of the chamber housed five inline stimulus projectors (IIE Model 107), arranged at the midpoint and four corners of a 12-cm square. Each projector was fitted with a transparent key which served as the response mechanism. Located below the projector array was a lever used to initiate a trial. Below the lever was a recessed light used to signal trial events. To the right and left of the light were speakers used to deliver the acoustic stimulus.

Banana-flavored pellets served as rewards and were delivered into a cup located on the right wall of the chamber. Chamber illumination was provided by an overhead 25-W bulb. A continuous source of white noise and a chamber exhaust fan, which together measured 85 db on the C-scale (slow-setting) of a Simpson sound level meter (Model 886) served to mask extraneous sounds. The programming of trial events, stimulus presentation, and data recording were controlled by a PC-XT computer.

The five stimuli consisted of a circle (A), 4-lobed pattern (B), picture of a monkey face (C), a 16-lobed pattern (D), and a vertical line (E). The forms appeared as white figures against a black background. The picture of the monkey face was in color.

Behavioral procedure

Shaping

The procedures were similar to those used by D’Amato and Colombo. The monkeys were first shaped to press the lever for reward. Next, pressing the lever resulted in illumination of stimulus A on one of the five projectors, which when pressed resulted in reward. Finally, pressing the lever turned on stimulus A which when pressed extinguished stimulus A and illuminated stimulus B, and press to stimulus B now resulted in reward.

Acquisition

Once shaped, the monkeys were trained on the AB, ABC, ABC and ABCDE series. With the exception of a brief familiarization period to be described, all items of the series were presented simultaneously. Although the order in which the stimuli needed to be pressed to achieve a reward remained constant across trials, the spatial position of the stimuli changed from trial to trial. All sessions consisted of 50 trials and the criterion for advancing to the new series was two consecutive sessions with at least 40 out of 50 correct responses.

Acquisition of a new series always began with a familiarization period in which only the items of the previous series were displayed simultaneously. A correct response to these items resulted in displaying the new stimulus, which if pressed, resulted in reward. For example, at the start of training on the ABCD series, only items ABC were displayed simultaneously. After correctly responding to these items, item D appeared, and a reward was delivered if the subject pressed item D. The criterion for this familiarization period was one session with at least 40 out of 50 correct responses. Once the subjects achieved this level, training continued with all the stimuli presented simultaneously.

Pairwise test

Following criterial acquisition of the ABCDE series, all subjects were given three pairwise tests, each separated by reacquisition of the ABCDE series. Each pairwise test consisted of 50 trials, five trials dedicated to each of the ten possible pairs.

Trial procedure

Following a 4-s inter-trial-interval (ITI), the recessed light began flashing at a rate of 5 cps indicating that the lever was enabled. Following two presses to the lever, the flashing stopped, the light remained on, and the stimuli appeared simultaneously on the projectors. The first correct response to each stimulus sounded a 1/6 tone. Repeated presses to the same stimulus were not considered errors but only the first press resulted in playing of the tone. A reward was delivered only following a correct press to the last item of the series.

In the case of the ABCDE series, a correct response was defined as pressing the five stimuli in the order A → B → C → D → E. Suc
Correct responses resulted in termination of the stimulus display, and entry into the ITI. Incorrect responses terminated the trial and began a time-out period signalled by extinguishing the recessed light. At the end of the time-out period, the recessed light was turned on signalling the start of the ITI. During the familiarization phase of each new series the time-out was set at 2 s. It remained at 2 s until the subject achieved a level of 25 out of 50 correct responses at which time the time-out was increased to 20 s.

Experimental design

The four animals were trained preoperatively on the ABCDE series and were then administered three pairwise tests, each separated by reacquisition of the ABCDE series. They were then removed from the task for a preoperative retention period of approximately 1 month and then retested on the ABCDE series. Two animals then received bilateral inferior temporal lesions and two received bilateral dorsolateral frontal lesions. Following a 2-week recovery period, the animals were retested on the ABCDE series and, if necessary, given remedial training described below. The postoperative pairwise test protocol was the same as described preoperatively.

Surgery

Prior to surgery the animals were treated with atropine (0.04 mg/kg, i.m.), anesthetized with ketamine (10 mg/kg, i.m.), followed by a minimum amount of barbiturate (Nembutal, average 5 mg/kg/h, i.v.) necessary to maintain the animal in the surgical plane of anesthesia.

For surgery, an incision was made in the scalp exposing the skull, and the cranium overlying the lesion site was removed. The dura was cut and retracted, and the cortical tissue removed by subpial aspiration with the aid of an operating microscope. The dura was then reapproximated and sutured and the scalp incision closed in anatomical layers. The animal was maintained in a heated padded recovery cage and observed until alert and mobile. Gentamicin sulfate (8 mg/kg, i.m.) was administered daily for a period of 1 week as a prophylactic measure against infection.

The intended inferior temporal lesion corresponded closely with area TE of von Bonin and Bailey. Laterally the posterior border began 10 mm anterior to a line drawn approximately parallel to the ascending portion of the inferior occipital sulcus, and the anterior border was close to the tip of the temporal pole. Ventrally the lesion extended to the occipitotemporal sulcus posteriorly and the anterior middle temporal sulcus anteriorly. Dorsally the lesion included both the lower bank and the fundus of the superior temporal sulcus along its entire anterior-posterior extent.

The intended dorsolateral lesion corresponded closely to area 9 of Brodmann. The posterior border extended from a line drawn perpendicular to the upper tip of the arcuate sulcus to its intersection with the sulcus principalis, and the anterior border was the frontal pole. Ventrally the lesion included both banks and the fundus of the sulcus principalis and dorsally the lesion extended to the midline.

Histology

Upon termination of behavioral testing, each animal was euthanized with an overdose of Nembutal followed by transcardial perfu-

Fig. 1. Cortical reconstructions for the two dorsolateral frontal and two inferior temporal animals with representative cross sections. The black area represents the extent of the lesion.
sion with normal saline followed by 10% formalin. After 1 week in 10% formalin, the head was mounted in a stereotaxic device and vertical and horizontal pins passed through the brain, the resulting tracks serving as reference points for the cortical reconstruction. The brains were removed and placed in a 30% sucrose 10% formalin solution and allowed to sink twice and then embedded in albumin/gelatin and sectioned at 50 μm with every tenth section mounted and stained with Cresyl violet.

RESULTS

Extent of lesions

The extent of the lesions for the two frontal and two inferior temporal animals are shown in Fig. 1. The frontal lesions extended to the midline and included both banks as well as the fundus of the principal sulcus. However, both frontal lesions were generally larger than intended with some damage ventral to the principal sulcus.

The inferior temporal lesions included most of the lateral cortex from the posterior middle temporal sulcus forward. There was slight damage to the temporal pole in both cases. In very few instances along the anterior-posterior extent did the lesions extend to the fundus of the superior temporal sulcus. In addition there was considerable sparing of inferior temporal cortex along the intended ventral areas of the lesion, especially in the region of the anterior middle temporal sulcus.

Performance on the ABCDE series

The number of trials to learn each series preoperatively and postoperatively for each animal are presented in Table I. Preoperatively, both lesion groups were well matched in terms of the number of trials to learn the ABCDE series, with the two frontal animals requiring a total of 6170 and 6829 trials and the two inferior temporal animals requiring a total of 7739 and 4053 trials.

Both frontal animals had little difficulty in relearning the ABCDE series postoperatively. In contrast, both inferior temporal animals were so impaired on the ABCDE task postoperatively that it was necessary to retrain them starting with the AB series. This difficulty manifested itself in two ways; over a 5- to 7-d period, neither animal attained more than 6.5% correct responses and neither animal was able to complete a full 50-trial session.

Despite their initial impairments, both inferior temporal animals eventually relearned the ABCDE task criterion levels. Postoperative retention for the AB, ABC, ABCD, and ABCDE series was assessed by the savings measure

preoperative trials – postoperative trials

and the results are shown in Fig. 2. Interestingly, for both animals the savings measure decreased uniform from almost 1.0 for the AB series to 0.13 (IT-1) and 0.23 (IT-2) for the ABCDE series, indicating that the subjects required almost as many trials to relearn the ABCDE series postoperatively as was required preoperatively.

Performance on the pairwise tests

The average performance over the three pairwise test sessions preoperatively and postoperatively is shown in Fig. 3. It is clear that neither frontal nor inferior temporal lesions had any effect on overall pairwise test performance.

As noted previously, the idea that imagery underlies performance of the pairwise test was based on the
findings that the latency to press the first item of a pair increased as a function of the position of that item in the series, and that the latency to press the second item increased in accordance with the number of missing items. We examined both first-item and missing-item latency effects in the present animals before and after the operations. The first-item latencies for each subject are shown in Fig. 4. For the most part, the trend of increasing latencies noted in the original D’Amato and Colombo study was replicated. Also clear is that with the exception of some alterations in the speed with which the task was solved, neither inferior temporal nor frontal lesions disrupted the first-item latency effect pattern. A randomized-block ANOVA applied to each subject’s data with operation (2: preoperative, postoperative) and first-item latencies (4: A, B, C, D) as factors confirmed that the interaction of these two variables was not significant (F-1, \( P = 0.24 \); F-2, \( P = 0.27 \); IT-1, \( P = 0.06 \); IT-2, \( P = 0.54 \)).

The missing-item latency effect was also replicated and the results are shown in Fig. 5. Again, a randomized-block ANOVA with operation (2: preoperative, postoperative) and second-item latency as a function of number of missing items (4: 0, 1, 2, 3) confirmed that neither frontal nor inferior temporal lesions significantly altered the pattern of the missing-item latency effect (F-1, \( P = 0.68 \); F-2, \( P = 0.82 \); IT-1, \( P = 0.19 \); IT-2, \( P = 0.95 \)).

**DISCUSSION**

Although only two monkeys served in each lesion group, the results obtained for each animal with a particular lesion were virtually identical. Lesions of the dorsolateral frontal cortex had no effect on retention of the ABCDE task or on performance of the pairwise test. On the other hand, performance of the ABCDE task was severely impaired following the inferior temporal lesions, and both monkeys had to completely relearn the task. Once relearned, however, the inferior temporal animals showed no impairment in performance of the pairwise test.

The finding that dorsolateral frontal lesions had no effect on performance of a serial-order task might appear at odds with findings from both human and monkey studies showing that frontal lesions impair judgements of serial order. In fact, frontal lesions appear to impair only performance of ‘internally ordered’ tasks in which the sequence either changes from trial to trial or the subject is required to monitor their responses and avoid choosing items previously chosen. ‘Externally ordered’ tasks in which one sequence is repeated without change, are not affected by dorsolateral frontal lesions in monkeys, at least when the series consists of two or three items. This study extends the finding that dorsolateral frontal lesions have no
effect on externally ordered tasks in monkeys with series of five items, or on externally ordered tasks when components of the series are absent, as was the case in the pairwise test.

In contrast to the absence of any effects following dorsolateral frontal lesions, inferior temporal lesions severely impaired performance of the ABCDE task. This impairment is most likely the result of a visual discrimination failure which is known to follow inferior temporal lesions in monkeys. In fact, the finding that overtraining in monkeys can insulate against the visual discriminative loss that follows inferior temporal lesions was also shown in this study in terms of the degree of savings in relearning the AB, ABC, ABCD, and ABCDE tasks. That savings were inversely related to series length was likely a reflection of the amount of overtraining received on the earlier components of the ABCDE series.

Contrary to our hypothesis, pairwise test performance, and in particular the first item and missing-item latency effects, were not affected by the inferior temporal lesions, suggesting that visual imagery was relatively intact. One possibility is that visual imagery was mediated by the spared inferior temporal tissue located along the dorsal and ventral borders of the lesion. This seems unlikely, however, since the lesions were of sufficient size to cause severe impairments on performance of the ABCDE task.

A second possibility was that the pairwise test did not tap visual imagery. Although this may be possible, the first-item and missing-item latency effects would be difficult to explain on terms other than the monkeys solving the task by forming a linear representation of the items and progressing through them in an orderly fashion beginning with item A. This notion is strengthened by the fact that similar representational schemes underlie judgements of serial-order behavior in humans, and furthermore, the latency relationships observed are similar to latencies observed in humans on tasks which engage visual imagery.

A third possibility why inferior temporal lesions had no effect on visual imagery may have been because we tested for visual imagery only after the subjects were extensively retrained and no longer showed any deficit on the ABCDE task. Had the monkeys been administered the pairwise test prior to relearning of the ABCDE task it is likely, especially given the degree to which performance of the ABCDE task was impaired, that deficits in visual imagery would have been evident. Indeed the fact that visual imagery was intact following relearning of the ABCDE task is in line with a number of studies in the human literature which show associations between the ability to recognize objects and the ability to image those same objects. For example, one visual agnostic patient who had difficulty in recognizing living but not non-living objects, was also impaired in imaging living as opposed to non-living objects. Thus to the extent that discrimination of visual stimuli is possible, then the results of this study indicate that imagery of those visual stimuli is also possible, and therefore this study supports the view that the neural mechanisms which mediate visual recognition are those which also mediate visual imagery.

If indeed visual imagery and visual recognition tap common neural substrates, then the area which mediates visual imagery following the inferior temporal (i.e. area TE) lesions is likely to be the same area which mediates relearning of the ABCDE task. In both monkeys with inferior temporal lesions, not only was striate cortex completely spared but so was most of the extrastriate cortex. Some time ago it was demonstrated that the tissue immediately posterior to inferior temporal cortex, now known as area TEO, mediates relearning of visual discriminations following inferior temporal lesions. Thus it is likely that this cortex may have mediated visual imagery of the five stimuli used in this experiment, as it was clear that this cortex must have mediated their discrimination.

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REFERENCES

9 Farah, M.J., Peronnet, F., Gonon, M.A. and Giard, M.H., Elec-