DISSOCIATIVE EFFECTS OF SELECTIVE LESIONS IN THE CAUDATE NUCLEUS OF CATS AND RATS 1

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Abstract. Lesions in the neostriatal region connected to the prefrontal cortex severely impaired delayed alternation in both cats and rats, whereas no such effect was found after damage to other neostriatal regions. These results indicate that the processes mediating delayed alternation are well localized in the neostriatum of both cats and rats. Two possible models of neostriatal functioning are discussed, one of functional heterogeneity, the other of functional homogeneity.

INTRODUCTION

Lesions in the head of the caudate nucleus in monkeys impaired the performance of the tasks sensitive to prefrontal ablations (2, 4, 6, 23, 24), while leaving the execution of other conditioned responses intact (1, 23, 24). It was further established that injury to different parts of the neostriatum of monkeys give separable behavioral effects (5, 13); these findings prompted the notion of functional heterogeneity of the neostriatum (8, 10, 22), and supportive data were obtained with other techniques (7) and nonprimate species (3, 9, 29, 38). The evidence seemed compatible with the suggestion that topical cortico–neostriatal connec-

1 This paper is dedicated to Professor J. Konorski. His eagerness to understand brain mechanisms led him to develop a neuropsychology concerned with “how it could be” rather than with “how it is” and inspired all who were so fortunate as to know him.

2 Previously R. G. E. Wikmark.
tions underlie the close functional relations between discrete cortical areas and associated sectors of the neostriatum (8, 10). However, in the experiment which suggested functional heterogeneity of the caudate nucleus in the monkey, lesions in two neostriatal regions severely impaired delayed alternation (DA) and damage to a third area caused a deficit in 2 of the 4 animals; only one lesion placement was without any effect on the performance of this task (13). These findings may be indicative of some, possibly "spatial", function common to several caudate regions (20). If the existence of such a factor could be firmly established, the notion of functional heterogeneity of the neostriatum would require important qualification. Therefore, we investigated here the effect of differently placed neostriatal damage on delayed alternation in rats and cats. In both species, it had already been shown that removal of the prefrontal cortex as well as injury to the associated part of the caudate nucleus impairs DA (11, 36). On the basis of the hodological-functional models earlier outlined we predicted that damage in caudate regions located outside of the projection field of the prefrontal cortex would cause no impairment in DA.

METHODS

Subjects were 13 male Wistar rats and 8 mongrel cats, 5 males and 3 females. The animals were maintained on approximately 90% of ad lib. weight through all phases of behavioral tests, and were fed once daily after training. Pairs of animals were housed in cages with water always available. The subjects were extensively handled before the experiment started. They were tested 7 days a week at approximately the same time each day. One tester trained all animals.

The rats arrived in the laboratory from a commercial breeder about ten days before training commenced. They were close to 3 months old at the start of the experiment. The cats were brought from private homes (mainly farms) and the exact age of an animal was not known, it was estimated to be 1–4 years.

Apparatus. The rats were tested in an open single-unit T-maze (start box, 20 cm; runway, 25 cm; arms, 32.5 cm) described in more detail elsewhere (36). Mashed rat-chow was kept at the end of each arm, behind a wooden barrier. The cats were trained in a variant of the Nencki Testing Situation (illustrated in 34). Briefly, a restraining cage was situated between two feeders placed 120 cm apart in a semicircular open field. The cage could be lowered (thus restraining the animal) and lifted (permitting free locomotion); it was made of wire mesh to allow the animal to see out. About 5 g of ground fish mixed with water and
canned cat-food was delivered into either feeder by a pump emitting a distinct sound. Two small light-bulbs mounted above each feeder could emit a flickering light. Both apparatuses were kept in dimly lit rooms and the cats were trained while a fan produced masking noise.

**Behavioral procedure.** The rats were trained in accordance with the method previously reported (36). Twenty-one trials were given in each session; the first response was always reinforced, and on all subsequent runs the animal was rewarded for alternating, whether or not the previous response was correct ("correction procedure", 37). Inter-choice time was close to 20 sec. Alternation led to access to the food for about 8 sec, while perseverative runs resulted in immediate removal from the maze. During intertrial intervals (about 8 sec following a correct response and 16 sec after an error), the animal was kept in a transport cage. Each rat was trained until it made 10 errors or less in 5 sessions (90% correct), and no more than 3 errors on any day. After a 10 day pause in training there was a five-session preoperative retention test, immediately followed by surgery. The animals were allowed a 10 day post-surgical recovery period before testing was resumed. Training continued as previously until the animal reattained the 90% criterion or for a maximum of 800 trials.

When the cats were first brought into the testing situation, both feeders were baited and the restraining cage was lifted. Alternation was reinforced from the beginning of training: having eaten one portion, the animal could find more food only in the opposite feeder, then again in the first feeder, and so on. As soon as the cat alternated promptly between the feeders, a flickering light was introduced as a signal for reinforcement. The light was activated when the animal had finished eating on the opposite side, and remained on until the signalled feeder was approached and food delivered. This training was continued until an animal alternated promptly in 20 successive runs. Discrete trials were then introduced; through gradual shaping the animal was trained to return to the center of the apparatus after each response, to accept restraining under the cage for 6 sec between successive responses, and to respond within 3 sec after the release. The flickering light was activated 3 sec before the cage was lifted and terminated either when S approached the other side, or when the food was delivered into the correctly chosen feeder. Intratrial correction runs were never reinforced, in this or later stages of the experiment. When the cat was well shaped, this "cued alternation" was given for 30 trials each day. On the first trial, the signal was presented on the side opposite to that visited on the previous day; on all subsequent trials, the "correct" feeder was that which was not visited on the previous trial (regardless of whether the last response
was rewarded or not). This training was discontinued when an animal made less than eight errors in 60 trials.

During delayed alternation proper, the flickering light was no longer used. Each session consisted of 31 trials. On the initial trial, either choice was rewarded; on subsequent runs, the cat was reinforced only for alternating. The intertrial interval (i.e., the duration of restraint) was kept at 6 sec. The interchoice interval varied across animals (depending on individual differences in speed of eating and latencies for choice and return) but remained fairly constant within subject. Training proceeded until an animal had committed less than 16 errors in 5 days and no more than 5 errors on any single session. After a 10-day pause in training, the animal received a preoperative retention test (5 sessions) and was operated on the following day. Ten days later, a postoperative retention test (5 sessions) began. Following this test, training was resumed with “cued alternation” as preoperatively, and then with uncued delayed alternation until the preoperative criterion was reattained.

Surgery. The rats were operated under Equithesin anesthesia (3.3 ml/kg intraperitoneally) and clean, but not sterile conditions. Before the operation each animal received 0.5 mg atropine sulphate intraperitoneally and 100,000 U of penicillin intramuscularly. The lesions were made stereotaxically; with bregma and the point just behind lambda kept at the same horizontal plane. A current of 2.5 ma was passed during 30 sec from the 1.5 mm uninsulated tip of a tungsten electrode, 0.4 mm in diameter, to a rectal plug at each of the points given in Table I. Lesions were placed in either of three regions of the neostriatum: anteromedial (AM; n=4), anterolateral (AL; n=3), or posterolateral (PL; n=3).

<table>
<thead>
<tr>
<th>AM</th>
<th>A₁</th>
<th>L₁</th>
<th>H₁</th>
<th>A₂</th>
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<td>2.2</td>
<td>5.0</td>
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<tr>
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<td>3.9</td>
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<td>−2.0</td>
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Sterile operations were performed on the cats under 35 mg/kg Nembutal injected intraperitoneally. Caudate lesions were made stereotaxically: the anteromedial sector (Ant.) was destroyed in 5 animals, and
a more posterior (Post.) region in 3 animals. On each side multiple
coagulations were made by passing 2.5 ma anodal d-c for 30 or 60 sec
through tungsten electrodes described above. The negative electrode was
attached to the skin retractor. The coordinates are given in Table II.

**Histology.** Deeply anesthetized animals were transcardially perfu-
sed with saline followed by neutral formalin. The brains were cut fro-
zen at 100 μm. Every fifth section throughout the lesioned area was
mounted, and camera lucida drawings were made from unstained sec-
tions.

**RESULTS**

**Anatomy.** In the rats, the only overlap between different lesions
was found at the level where the anterior commissure crosses the midli-
e (Fig. 1). All lesions involved variable amounts of capsula interna and
corona radiata. In two animals with AM lesions the septum was super-
ficially damaged, and all PL lesions involved the globus pallidus (Fig.
1). In the cats, no overlap was noted between Ant. and Post. lesions
(Fig. 2). Fiber bundles passing around and through the caudate were
more extensively damaged after Ant. than after Post. lesions. One cat
with posterior lesions had developed bilateral oedema causing defor-
mation of the brain and damage to the marginal and suprasylvian gyri
due to pressure.

**Behavior.** The rats with anteromedial lesions showed severe losses
in the postoperative retention tests, the animals in group AL were less
impaired, and Ss with PL damage performed without deficit (Fig. 3).
Group AL promptly regained the preoperative performance level; in con-
trast, three of the four Ss in group AM failed to reach criterion within
800 trials (Fig. 4). There was no overlap between the groups on any
measure.

**Table II**

Coordinates for stereotaxic lesions in either of two caudate regions in cats. All distances in mm.

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<tr>
<th></th>
<th>A₁</th>
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<td>1.0</td>
<td>1.0</td>
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<td>2.5</td>
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<td>3.5</td>
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<tr>
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<td>12.0</td>
<td>5.5</td>
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Fig. 1. The three kinds of caudate lesions superimposed on one set of standard drawings from atlas of König and Klippel (16). The smallest (solid black) and the largest (lines) extent of damage on each level is indicated. Vertical lines, anteromedial lesions; horizontal lines, anterolateral lesions; dots, posterolateral lesions.

All cats sustaining injury in the anteromedial portion of the caudate showed postoperative retention losses. All three Post. cats performed at criterion level (90% or better) in the retention test. Only the animal with brain deformation following posterior damage showed an indication of a loss, (preoperative retention: 3 errors, postoperative retention: 15 errors). There was no overlap between the groups, as seen in Fig. 5. The effect of anterior caudate damage was quantitatively similar to that of prefrontal excision in a group of animals tested concurrently for other purposes (R. G. E. Öberg and I. Divac, in preparation), whereas posterior damage was as ineffectual as ablation of the middle suprasylvian gyrus (Fig. 5). All Ss with anterior caudate lesions relearnt the task, two of them with savings (median trials preoperatively: 540, postoperatively: 540).
Fig. 2. Lesions in two loci within the caudate nucleus of cats illustrated on standard diagrams. The smallest (solid black) and the largest (lines) lesion on each level is given. Horizontal lines, anteromedial lesions; vertical lines, posterolateral lesions.

Fig. 3. The difference in number of errors between the preoperative and the postoperative retention tests (100 trials each) for individual rats of three groups. A high positive value indicates a large increase in incorrect responses following surgery.
Fig. 4. The effect of lesions on delayed alternation in the three groups of rats (PL, AL and AM). The entire bars indicate the number of trials to postoperative criterion; checkered areas illustrate the number of errors. F, failure to relearn within 800 trials.

Fig. 5. The difference in errors between preoperative and postoperative retention tests (150 trials each) in four groups of cats. Animals with cortical ablations included for comparison: PF, prefrontal cortex (black triangles); SS, suprasylvian gyrus (white triangles); ant., anteromedial caudate nucleus (black circles); post., posterior caudate nucleus (white circles). X denotes the cat with brain edema.
DISCUSSION

In these experiments, destruction of the neostriatal projection field of the prefrontal cortex severely impaired DA in both cats and rats. In neither species did caudate lesions outside of this field produce any marked impairment. The mild deficit seen after anterolateral injury in rats may be attributed either to marginal encroachment upon the poorly defined projection area of the anteromedial prefrontal cortex, or to some involvement in DA of the suprarhinal cortex and its associated neostriatal region. At any rate, the present findings gave no support to the possibility of one widely distributed function of the neostriatum as expressed in alternation behavior. The findings in monkeys (13) may also have alternative explanations. Lesions aimed at the tail of the caudate nucleus involved some hippocampal tissue and hippocampal lesions alone impair DA in some monkeys (32). The posteroventral lesions, on the other hand, might have disconnected the cortical dorsolateral region from mesencephalic afferents.

Extending the generality of previous data, (3, 5, 9, 13, 29, 38), then, the present findings show that the effects of caudate lesions depend on the locus of the injury, much as the results of cortical damage are determined by its localization. This evidence is suggestive of specialization of function within the neostriatum, but alternative explanations are possible.

One of these alternatives has concerned us for some time (10, 12, 34, 35): the different behavioral syndromes may be the effects of differential cortical undercutting rather than of selective caudate destruction. This problem will be further treated elsewhere (R. G. E. Öberg and I. Divac, in preparation). Suffice it to say here that there are strong reasons for believing that the neostriatum per se is essential for alternation behavior. If we accept the role of the neostriatum in DA, we can proceed to evaluate the evidence for further localization of this role within the nucleus.

The demonstration that a substantial portion of the caudate can be destroyed without any effect on DA proves, at the very least, that this behavior does not require proper functioning of the entire structure. The concurrent demonstration of the critical importance of the site of damage can, however, be explained in different ways. Very schemati-

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3 Strong evidence was obtained in a series of studies (35) showing that destruction of the anterior part of the neostriatum permanently impaired DA (tested as presently) even in rats which had relearned the task following anterior and medial decortication — and in which therefore no cortex remained to be disconnected. (See also 14).
cally, these results would be compatible with either of two models describing the modus operandi of the neostriatum; both models would be consonant with the known cytological (15) and biochemical (18, 33) homogeneity of the structure.

According to the first model, the neostriatum consists of a number of largely independent units: different units are recruited for different purposes and there is little redundancy in processing. Different neostriatal sectors receive different information from different neocortical (and thalamic) regions, process this information locally, and forward their output in separate and noninterchangeable channels. The concepts of "mass-action" and "equipotentiality" are no more applicable to the neostriatum than to the neocortex. The anteromedial portion of the caudate in rats and cats forms a distinct functional unit with the prefrontal cortex: this, and only this, region of the caudate ever constitutes a part of the system subserving DA and similar behaviors (25).

In the second model, the neostriatum is conceived of as a unitary device: any part of the formation plays the same behavioral role(s) as any other part. There is a great redundancy in its operations, and there are many interchangeable output channels; thus, only a portion of the nucleus needs to be operative for any behavior to appear normal. The structure plays a role in many different behavioral functions, and for different functions it depends on different instructions or information. The source of the critical information is in each case that cortical (and/or thalamic) region which — in another way — subserves the same behavior. Different cortical (and thalamic) regions have access to the neostriatum; they "enter" that part of the neostriatum which is most closely situated, but the information is distributed to all intact parts of the nucleus. When a channel of afference is interrupted, by lesion or by electrical stimulation, the neostriatum can no longer take its part in the behavioral function(s) for which that information is required, even if the necessary number of local circuit- and efferent neurons is preserved. The reason why a lesion in the anteromedial neostriatum in cats and rats effectively disrupts DA while lesions in other sectors do not, is that only this particular anterior placement disconnects the neostriatum from the prefrontal cortex (the mediodorsal nucleus).

The two models constitute extremes with respect to regional specialization within the neostriatum. According to the second model, the

4 There is suggestive evidence (see review to date in 10) that at least some "specific" thalamic nuclei project topically to the neostriatum. This possibility needs to be further explored; it carries important implications for possible instances of neostriatal autonomy from the neocortex.
structure is functionally homogeneous, according to the first model the structure is functionally heterogeneous. The true state of affairs may well be found somewhere between these alternatives, and it is possible that the neostriatum works more "as a whole" while mediating certain functions, while subregions may be selectively recruited for other functions. At present, there are insufficient data to adopt either model. Studies of electrical and chemical activities in different parts of the neostriatum during the same behaviors could provide valuable information, as would investigations of the effects of interruption of pathways between neocortical and neostriatal areas. Anatomical and physiological assessment of discreteness versus convergence of the efferent from different parts of the neostriatum will shed important light on the problem.

**Note added in the proofs**

In *Journal of Comparative and Physiological Psychology* 1975, 88: 342–354, Livesey and Rankine-Wilson described impairment in delayed alternation produced by brain stimulation in cats. The electrodes were placed in or near the caudate region which in the present experiment seemed uninvolved in performance of delayed alternation. Since other regions in the caudate nucleus were not explored and thresholds measured, the stimulation might have produced the effects by spreading to the prefrontal cortex, the associated part of the caudate nucleus, or some of their connections.

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5 The lack of long fibers interconnecting caudate subregions. (15) as well as electrophysiological evidence suggesting little spread of activity between different sectors (21, 30) seemingly favor the first model. The apparent point-to-point arrangement of the output path(s) from the neostriatum to the pallidum (19, 26, 27, 28, 31) as well as from pallidum to the VA/VL complex (17) suggests that separate efferent channels are, at least, possible. Finally, the high degree of redundancy necessarily implicit in the second model seems somewhat implausible.

6 The ideal experiment would involve disconnection between neocortex and neostriatum without damage to either structure or to fibers connecting these structures with other parts of the brain. Such a lesion is hardly possible to achieve; an approximation may be accomplished by interruption of the subcallosal fasciculus as far anterior as possible in the monkey.
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