FUNCTION OF CINGULATE AND PREFRONTAL CORTEX IN FRUSTRATIVE BEHAVIOR[1]

John S. STAMM

Department of Psychology, Queens College, Flushing 67, New York, U.S.A.
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Ever since P a p e z (1937) proposal for a neural mechanism of emotion investigations have been conducted to clarify the behavioral functions of neural structures within the rhinencephalic system. Supporting evidence for P a p e z thesis has been derived from behavioral changes following amygdalectomy in monkeys, especially with regard to aggressive behavior (K l ü v e r and B u c y 1939) and dominance status (R o s v o l d et al. 1954). Ablations of cingulate cortex, however, has not been found to affect aggressive or dominant behavior in monkeys (P r i b r a m and F u l t o n 1954; M i r s k y et al. 1957) and, as stated in a recent review article „...as regards the anterior cingulate region, renewed studies find as yet no conclusive evidence to substantiate the earlier claims of the importance of this area in emotion" (K a a d a 1960, p. 1368). A clue to the possible implications of cingulate cortex in behavior has been reported by P r i b r a m and F u l t o n (1954) who observed shortened duration of avoidance behavior in a „frustrating" situation after cingulectomy. These authors observed similar reactions in a monkey after ablation of dorsolateral frontal cortex.

The present experiment was designed to investigate more systematically the role of cingulate cortex with regard to frustrative responses. Frustration has been conceptualized (A m s e l 1958) as an implicit reaction elicited by non-reward after a number of prior rewards. In the normal animal the withholding of a reward after training which leads to

the expectation of rewards results in a frustrative behavior. The experimental requirements for eliciting frustrative responses might be met by the operant schedule of reinforcement, labelled DRL (differential reinforcement at low rates, W i l s o n and K e l l e r 1953). On this schedule an animal receives a reward for pressing a lever, provided it has refrained from responding for a predetermined delay period. If it presses too soon, the reward will be further delayed. By first training monkeys on the DRL schedule with a short delay setting, so they obtain a high ratio of rewarded responses, and then suddenly lengthening the delay, frustrative responses might be elicited following lever presses which had previously been rewarded.

This experimental design has been followed in the present experiment with cingulectomized and normal control monkeys. Because of the observations by P r i b r a m and F u l t o n (1954) and the clinical interest in prefrontal lobe functions, monkeys with ablated dorsolateral prefrontal cortex were also tested.

MATERIAL AND METHODS

Subjects. Three groups of immature monkeys were used-four monkeys (*Group C*) that had been subjected to bilateral ablations of cingulate cortex, six monkeys (*Group F*) that had had bilateral ablations of dorsolateral prefrontal cortex, and six normal controls (*Group N*). All of these subjects had been used in a previous experiment on timing behavior (S t a m m 1963).

Apparatus. The subject was tested in a portable cage (16″ × 13″ × 22″ high), that was placed in a sound-absorbing converted icebox. The front of the cage faced a white lucite panel, from which a lever protruded one inch into the cage. A food cup was beneath the lever. A dim overhead light provided constant illumination, and blower provided air circulation and a masking noise.

Control and recording panels were located in an adjacent room. The subjects were trained on the DRL schedule of reinforcement. For this schedule the first lever press in each session was rewarded with a 48 mg. dextrose pellet, and subsequent presses were rewarded only if they occurred after a predetermined delay period. If the monkey pressed during the delay, the timer reset so the subject had to wait until the delay terminated before it could receive a reward. Concomitant with each reward a white light behind the lucite panel was turned on for two seconds. Responses and rewards were recorded on counters, a cumulative recorder, and an Esterline Operation Recorder.

Procedure

Prior Training. In the previous experiment (S t a m m 1963) the subjects had been trained on the DRL schedule with gradual delay increments. They were first tested on 10 sec. delay settings until they met the criterion of 50% rewarded responses during each of three consecutive sessions or during the first, second, and

fourth of four consecutive sessions. On the following day the delay was increased to 15 sec. and training continued to criterion. This procedure of step-wise increments by 5 sec. was continued to the maximum setting of 70 sec. delay or until a subject failed to meet criterion. If a subject did not meet criterion performance after 25 sessions on a delay setting, that delay was increased by 5 sec. and testing continued for a maximum of 15 sessions. Monkeys which did not meet criterion on that delay were considered to have failed.

In that experiment all subjects met criterion on the 25 sec. delay setting, but on longer delay settings subjects in each group failed. On the 70 sec. delay criterion was met by only two normal and three prefrontal monkeys.

Present Experiment. On the day following completion of the prior training, each subject was tested on the DRL schedule, with a delay setting 60 sec. longer than that on which it had previously met criterion performance. Consequently, delay settings for individual subjects were from 85 sec. to 130 sec. Fifteen consecutive daily sessions were given, each of 80 or 100 min. duration, depending upon the length of the delay setting.

RESULTS

Anatomy. The surgical procedure and landmarks for cingulate ablations were similar to those previously described (P r i b r a m and F u l t o n 1954), except that resection of cingulate cortex continued posteriorly, approximately to the level of the splenium of corpus callosum. Reconstructions of these ablations (Fig. 1) show nearly complete destructions of cingulate cortex, with occasional damage to adjacent cortical structures and to corpus callosum.

The intended limits for dorsolateral prefrontal ablations were from frontal pole to anterior bank of arcuate sulcus, and from midline to orbital surface, including the banks and depth of principal sulcus. Reconstructions of the brains indicate complete ablations within these limits for all subjects, except for one where the tip of one frontal pole was spared.

Behavior. The two normal and four prefrontal monkeys, which in the previous experiment (S t a m m 1963) had met criterion on the 70-sec. delay, were tested on 130-sec. delay. For the other subjects, delay settings were between 85 and 120 sec. Because of the procedural requirements in the previous experiment differing numbers of training sessions had been given to individual subjects before the 60 sec. delay increment. There were, however, no systematic differences among the experimental groups in the amount of prior training, as seen by median scores (Table 1), or in the ranges of scores for subjects within each group, which were from 80 to 160 sessions (except for one normal monkey, 71 sessions). Also, there were no systematic differences in the amount of prior training between the groups of monkeys tested on 130 sec. delay and on shorter delay set-

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tings. The response patterns for each subject stabilized during the
course of testing, so quantitative analyses were based on the subjects'
performance during the final four testing days.

The records of responses frequently revealed episodes of two or more
lever presses in rapid succession. Responses which occurred after inter-
response intervals of two seconds or less were scored as *multiple presses*,
while responses after longer intervals were considered *timing responses*.
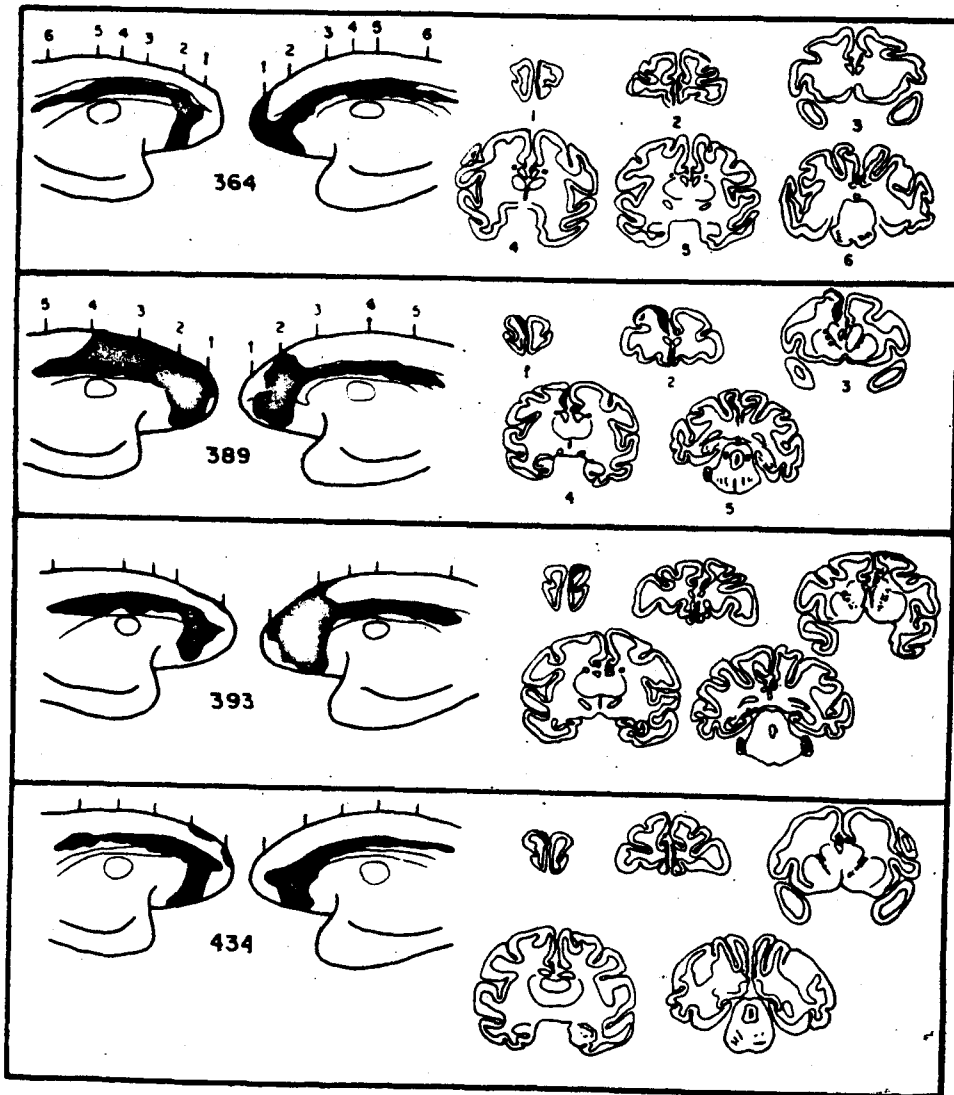

Fig. 1. Reconstructions of cingulate ablations. Ablated areas are indicated in black.
For each brain the cross-sections correspond to the levels indicated for #389

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The proportion of multiple presses to total number of responses was appreciably higher for the normal than for the brain-lesioned monkeys. Group medians of these proportions are indicated in Table I and represented by Fig. 2. For individual subjects scores ranged from 10.8 to 23.8 for Group N, 1.7 to 10.0 for Group C, and 1.1 to 9.2 for Group F. The higher incidence of multiple presses for normal monkeys is statistically highly significant (Mann-Whitney U-test, $p < .001$).

Table I
Results — (Group Medians)

Group	No. Sessions-Prior Training	Multiple Press[1]	Reward[2]
Cingulate	113	4.1	13.6
Prefrontal	111	5.6	18.4
Normal	128	16.1	9.2

1 percent multiple presses of total responses
2 percent rewards of timing responses

Multiple presses occurred, moreover, predominantly after nonrewarded lever presses, as seen by the following analyses. Each subject's response records were examined for multiple press episodes on the eight alternate sessions during the 15 session period. For responses following rewards the median incidence of these episodes was 2.5 per cent of
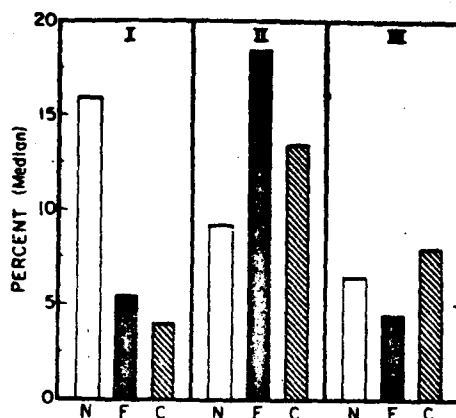

Fig. 2. Percent of group medians for. (I) multiple presses to total number of responses; (II) rewards to timing responses; and (III) responses after interresponse times longer than twice the means. N, normal group, F, prefrontally ablated group, and C, cingulectomized group

rewarded responses for Group N, 0.4 per cent for Group C and 1.5 per cent for Group F, whereas the medians of multiple press episodes were 15. per cent of nonrewarded timing responses for Group N, 5. per cent for Group C, and 6. per cent for Group F.

The rates of rewarded responses, as percentages of timed responses, resulted in higher median values for the cingulate and prefrontal groups

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than for the normal group (Table I and Fig. 2). There was considerable overlap, however, among reward scores for subjects in these groups, so group differences were statistically not significant.

The distributions of interresponse times (of timing responses) are presented in Fig. 3. The distributions in the left column are means for two subjects in each group on delays of 85 or 90 sec., those in the middle co-
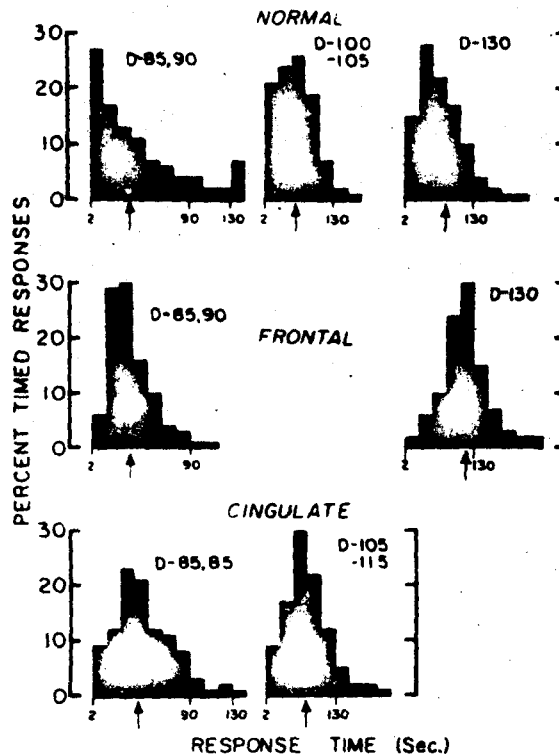

Fig. 3. Interresponse time distributions (of timing responses) during last four sessions. Means for subgroups on delay settings (D) indicated. Arrows indicate mean interresponse times. Units of interresponse times are 12.8 sec. for left hand column and 25.6 sec. for other distributions

lumn are for two normal and two cingulate monkeys on delays near 105 sec., and the graphs in the right column are for the two normal ánd three prefrontal subjects tested on 130 sec. delay. The distributions for the normal monkeys express marked disruptions of timing behavior, with high proportions of very short and very long (more than 130 sec.) interresponse times. By contrast, the prefrontal and cingulate groups obtained

relatively adequate timing distributions. Although the normal and pre-
frontal subgroups tested on 85 or 90 sec. obtained the same mean inter-
response time (32 sec.), the shapes of the two distributions differ mar-
kedly.

The degree of positive skewing of the distributions may be expressed
by the proportion of timing responses longer than twice the median in-
terresponse time for each subject. Medians of these indices for the three
groups, as represented in Fig. 2, indicated no marked differences among
the groups. However, the three prefrontal subjects that were tested on
the 130-sec. delay obtained lower indices (1.3 per cent to 3.4 per cent)
than did any of the normal monkeys.

On the 130-sec. delay setting marked differences were obtained in
the IRT distributions between the normal and prefrontal subgroups
(Fig. 3). The mean IRT (67 sec.) for the two normal monkeys on this set-
ting was shorter than the mean IRT (76 sec.) which these subjects had
obtained on the previous 70-sec. delay setting. By contrast, the three
prefrontal monkeys, whose mean IRT on the 70-sec. delay was 72 sec.,
were able to adapt their responses on the final 130 sec. delay, so that
they obtained a mean IRT of 112 sec. The shift in mean IRT by the pre-
frontal monkeys from 72 to 112 sec. is statistically significant (t-ratio =
= 17.7; p $\langle$.01).

DISCUSSION

The outstanding finding in the present experiment is the higher in-
cidence of multiple presses by normal than by the brain-damaged mon-
keys. High proportions of short interresponse times (below two seconds)
seem to be characteristic for interresponse time distributions on the DRL
schedule for rats (S i d m a n 1956) and for monkeys (B r a d y 1960).
But the incidence of these short interresponse times is also dependent
upon the experimental procedure, as has been discussed in a previous
communication (S t a m m 1963), because they occur only rarely under
the procedure of gradual delay increments.

The finding that multiple presses were emitted predominantly after
nonrewarded responses satisfies A m s e l's (1958) requirements for the
conditions eliciting frustrative responses. We observed, furthermore: (a)
that multiple presses generally did not occur after the first nonrewarded
response following a reward; (b) that multiple presses were frequently
succeeded by short interresponse times or by bursts of lever presses in
rapid succession; and (c) that the subjects during multiple press episodes
exhibited gross „emotional" behavior patterns, as expressed by hyperac-

tivity, yelling, or banging on cage and apparatus. Consequently, the rate of multiple presses may be considered as an index of frustrative behavior.

No systematic behavioral differences were obtained in the present experiment between the cingulectomized and prefrontal lobectomized groups of monkeys. This finding agrees with the report by P r i b r a m and F u l t o n (1954). The anatomical connections between these two cortical structures might be responsible for the lack of differential results between the two experimental groups.

The present findings of lower rates of frustrative responses by the cingulectomized and prefrontal lobectomized monkeys are in agreement with the earlier observations by P r i b r a m and F u l t o n (1954). These results, point to relatively subtle behavioral differences between normal and brain damaged monkeys, since the latter subjects showed no marked impairment in meeting the experimental requirements and exhibited no gross emotional disturbance, such as excessive fear or aggressiveness toward the experimenter. Similar findings by M i r s k y et a l. (1957) lead to the conclusion that cingulectomy in monkey does not necessarily result in disturbed emotional behavior. In contrast to these reports, cingulectomy has been found to greatly increase the dog's savageness and aggressiveness toward man (B r u t k o w s k i et a l. 1961) and to markedly impair hoarding (S t a m m 1954) and disrupt maternal behavior (S t a m m 1955) in rats. The differing consequences of cingulectomy may of course be related to species differences. However, consideration should also be given to the environmental conditions which may affect the behavioral consequences of brain damage. The monkeys in the present and the previous investigations had had a great deal of experience in the experimental situation before they were tested for emotional responses and in the social experiment a stable dominance hierarchy had been established prior to cingulectomy. In the hoarding experiment, the cats also had a certain amount of preoperative testing, whereas in the maternal experiment the rats had only limited prior experience, by having given birth to one litter each before cingulectomy.

The increased threshold for frustrative responses found in the present experiment would implicate cingulate and prefrontal cortex in the neuronal control of emotional behavior. Primary motivation by the brain damaged subjects, however, was not markedly impaired, since their rates of timed lever presses were not below the rates by normal controls and they actually obtained more rewards than did the normal monkeys. The function of cingulate cortex may be related to the functions of other rhinencephalic structures, because of the extensive anatomical interconnections in this neuronal system. G l o o r (1960) assigns to the rhinence-

phalic system functions of modulating primary motivational activities which are integrated in subcortical structures. With regard to the amygdaloid structures ´G l o o r (1960) concludes that the basic defect resulting from amygdaloid lesions „could be described as a disturbance in those motivational mechanisms which normally allow the selection of behavior appropriate to a given situation" (p. 1416). He therefore considers these structures to be implicated in „motivational selection". It is then conceivable that cingulate cortex and related structures function in a second motivational modulating system, which serves to maintain a high state of drive. This hypothesis might explain the present paradoxical finding of superior performance by the brain-damaged subjects. The higher drive state in the normal subjects under the conditions of motivational conflict resulted in frustrative responses, which in turn interfered with efficient performance. The more precise functions of this motivational modulating system in relation to frustrative situations need to be examined by further experimentation. Of particular relevance will be the interactions between the experimental conditions and motivational variables in evaluating the consequences of cingulectomy.

SUMMARY

Three groups of monkeys — 4 subjects with ablated cingulate cortex, 6 subjects with ablated prefrontal cortex, and 6 normal controls — were tested on the operant DRL schedule. On this schedule a food reward is given for a lever press, provided no response had been given for a predetermined delay period. If the lever is pressed during the delay, the subject has to wait again for the period of the delay in order to receive a reward. All subjects had prior training with the DRL schedule, under conditions of gradual delay increments (S t a m m 1963). The experimental testing was with a delay setting 60 seconds longer than the last setting on which the subjects had prior training. Fifteen daily sessions were given.

The response records revealed episodes of *multiple presses*, i.e. responses which occurred within 2 second intervals. The normal monkeys responded at significantly higher rates of multiple presses than did either of the braindamaged groups. No significant differences were obtained between the cingulectomized and prefrontal lobectomized groups. Interresponse time distributions revealed clearer timing responses by the ablated than by normal subjects.

Analyses of the results indicate that multiple presses were expressions

of frustrative behavior. The paradoxical finding of superior performance by the brain-damaged monkeys is interpreted in terms of motivational function of cingulate cortex. It is proposed that this neuronal system serves to maintain a high drive state in the organism.

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