Behavioural changes after ablation of subdivisions of the rat prefrontal cortex

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Abstract. Sham operated controls and four groups of rats subjected to ablation of various parts of their frontal cortex were compared in food and water intake and four behavioural tasks. The ablations were aimed at removing (1) the ventral prefrontal cortex, (2) the dorsal part of the medial prefrontal cortex, (3) the total medial prefrontal cortex, and (4) the anterior dorsolateral (non-prefrontal) cortex. Only two groups had a significantly impaired food and water intake: the ventral prefrontal and the non-prefrontal anterolateral. The latter group was not adipsic. Two variants of spontaneous alternation were administered in a T-maze: a non-cued version in which both arms were grey and a cued version in which one arm was white and the other black. While all ablated groups behaved like the control group on the non-cued test, the number of perseverative responses of the total anteromedial group was significantly increased in the cued version of the test. Significant group differences could be seen neither in a test of conditioned taste aversion nor in extinction of operantly conditioned bar presses. Finally, in a vertical hole-board exploration test the only significant group difference was a prolongation of the mean visit duration of the ventrally lesioned animals in comparison with all other groups. The results of the present study further indicate functional differentiation within the prefrontal cortex of the rat.

Key words: prefrontal cortex, rat, food intake, water intake, spontaneous alternation, conditioned taste aversion, extinction, exploration, vertical hole-board
INTRODUCTION

In the present study we are continuing the analysis of behavioural functions of the rat's prefrontal cortex (PFC) aiming to provide data useful in species comparisons. The aim was approached by selection of both the areas to ablate and behavioural situations in which the animals were studied.

Anatomical considerations (Divac et al. 1978, see also Mogensen and Divac 1984) made us suggest that the orbital area in the monkey corresponds not only to the rat suprarhinal area of Leonard (1969) but includes also the ventral surface of the frontal pole in front of the fusion with the olfactory nucleus as well as the ventral portion of the mesial cortex. This ventral area in the rat includes first parts of the insular cortex innervated by the mediodorsal thalamic nucleus (Divac et al. 1978; similar results are obtained by Reep and Winans 1982, in another rodent, the hamster) and, secondly, the "ventrolateral orbital area" of Groenewegen (1988) which may not receive projections from the mediodorsal thalamic nucleus (Krettek and Price 1977, Groenewegen 1988). The dorsal part of the mesial prefrontal area seems to correspond to collapsed dorsal mesial and the medial part of the dorsolateral PFC in monkeys, including the frontal eye field (Divac et al. 1978). These anatomical relationships and the technical difficulties of selective ablations of the ventromedial part of the frontal pole were the reasons to make three lesions of the PFC: (I) the ventral prefrontal cortex (described above), (2) the dorsal anteromedial cortex, and (3) the total anteromedial cortex. By studying this combination of ablations we hoped to gain a better understanding of the functions of the ventromedial frontal cortical ridge. Furthermore, in one group of rats the anterior dorsolateral cortex was removed. This area does not receive projections from the mediodorsal nucleus and consists roughly of the premotor area and the face region of somatosensory and motor cortex. This area is often damaged in attempts to ablate the suprarhinal cortex. The four groups of rats with cortical ablations and the sham operated control group were compared in postoperative food and water intake and four behavioural tasks.

Impaired food and water intake were found in rats with lesions including the suprarhinal part of PFC (Kolb 1974a, Kolb and Nonneman 1975, Kolb et al. 1977) while no such impairment seems to follow ablation of the anteromedial cortex (Kolb 1974a, Kolb and Nonneman 1975). We were mainly interested in the behaviour of the ventral and dorsolateral groups in order to separate contributions of these areas to aphagia.

Conditioned taste aversion was neither affected by suprarhinal nor mesial frontal ablations (Divac et al. 1975a). Presently, we wanted to study whether ablation of the entire ventral cortex would induce an impairment in conditioned taste aversion, thus giving support to Nauta's (1971) notion of "interceptive agnosia".

In rats subjected to ablations of the ventral prefrontal cortex or the dorsal medial prefrontal cortex we failed to see any effects on two measures of behavioural extinction (Mogensen and Divac 1984). However, Kolb et al. (1974) found ablation of the suprarhinal part of the prefrontal cortex to impair significantly extinction of operant responses while lesions of the total anteromedial cortex failed to interfere with extinction (Schwartzbaum et al. 1964, Kolb et al. 1974, Nonneman et al. 1974, Mogensen and Divac 1984). These discrepancies made us reproduce as closely as possible the behavioural situation which was sensitive to orbital lesions in the monkeys (Butter 1969) and test our groups in this task.

Spontaneous alternation has been found impaired (e.g. Divac et al. 1975b) or unimpaired (e.g. Mogensen and Divac 1984) after prefrontal ablations. In an attempt to find an explanation for this discrepancy, we performed the spontaneous alternation test in both a normal, uniformly grey, T-maze and in a similar maze in which one of the arms was black while the other was white. The procedure did not differ from that used in our previous study (Mogensen and Divac 1984). The "cued" version of spontaneous alternation was performed after the "non-cued" version.
Finally, we exposed the animals to a newly developed test of exploratory behaviour: the vertical hole-board exploration test (Iversen and Mogensen 1988). This test allows automatic recording of "temporal" as well as "spatial" aspects of rats' spontaneous exploration of a vertical matrix of 54 evenly spaced holes. The test appears to belong to the category of tests that are able to reflect exploratory behaviours in a manner that is relatively independent of changes in "locomotion" (e.g. J. Mogensen, T.K. Pedersen and S. Holm in press). In previous experiments the vertical hole-board exploration test has been found able to reflect in a sensitive manner the behavioural consequences of a broad spectrum of neural manipulations (e.g. Iversen and Mogensen 1984, 1988, Geoffroy and Mogensen 1988).

METHODS

Apparatus

The two variants of spontaneous alternation were studied in an open, grey, plastic, one-unit T-maze with 21.2 cm high walls and 10.0 cm wide corridors. The stem was divided by a guillotine door into a 19.7 cm long start box and a 24.7 cm long runway. The length of each arm was 31.3 cm. The wall at the end of each arm consisted of a lower, 7.0 cm high, metal part (where in certain experiments a guillotine can be inserted) and a higher 14.2 cm plastic part of the same colour as the rest of the maze. For the non-cued spontaneous alternation the maze was used as described above. For the cued spontaneous alternation procedure, however, each arm received three 0.5 cm thick and 21.2 cm high plastic inserts: one, 10.0 cm wide covering the end wall and two 29.5 cm long covering each of the side walls. The inserts placed in the left arm were black, those inserted into the right arm were white, thus making all walls of the left arm black and all walls of the right arm white. The maze was placed in the middle of a well lit room.

The extinction experiment was performed in operant conditioning units - the "Student Research Model" of Ralph Gerbrands Company. Details of this equipment have been given previously (Mogensen and Divac 1984). Solid state equipment controlled the experiment and recorded the bar presses.

For the exploration experiment a vertical hole-board apparatus was used. One semiopaque 8 mm thick wall in a 25.6 cm wide, 26.5 cm deep, and 22.5 cm high opaque chamber had 54 1.7 cm diameter holes (arranged in 6 horizontal and 9 vertical lines). The center to center distance between holes was horizontally and vertically 2.5 cm and diagonally 3.5 cm. The top of the box also served as door to the chamber. The floor of the chamber consisted of a wire grid. The wall containing the holes had a grid of 3 mm wide channels imbedded in it. Each channel had an infrared LED (light emitting diode) at one end and a photocell at the other end. The grid was arranged in such a way that each hole contained the crossing of one horizontal and one vertical line at its center. Nose-poking would break the infrared light beams of the two channels. The photocells were connected to an interface card through which the data were collected by a TIMEX-computer. A detailed description of this apparatus has been published separately (Iversen and Mogensen 1988). The hole-board apparatus was situated in the middle of a well lit, sound shielded room in which no other activities took place during testing.

Subjects

Forty male Wistar albino rats with a history of bar pressing on a CRF-schedule in operant chambers similar to those used in the present experiment served as subjects. The rats weighed approximately 300 g at the beginning of the experiment. They lived in single cages in a room kept on a 12 h light/dark cycle (on 6.00 h; off 18.00 h). Except during the taste aversion experiment water was always available. The rats were fed commercial rat chow which was always available except for the deprivation period of the extinction experiment and the 24 h preceding the exploration test. During the deprivation period the animals were fed once daily (after training) and were maintained at approximately
80% of ad libitum body weights. The rats were randomly divided into five equal groups: sham operated controls, and four groups with ablation of either ventral, dorsal anteromedial, total anteromedial prefrontal or anterolateral non-prefrontal cortex. One animal with lesion of the dorsal anteromedial cortex became ill in the interval between the extinction and exploration experiments and had to be sacrificed. Since no signs of disease had been observed in this animal up to and including the extinction experiment, the data from the prematurely sacrificed animal was included in the statistical analysis.

**Behavioural procedure**

**GENERAL PROCEDURE**

All animals were weighed on the first day of the experiment and on the following day subjected to surgery. The day of surgery was also the first day of the food and water intake experiment. This experiment continued until the animal had reached a body weight at least equal to the preoperative weight. When this weight had been attained the animal was left for at least 25 days without any training or testing. After this pause the first session of the non-cued spontaneous alternation test was performed followed by a 5 days pause upon which the second session of non-cued spontaneous alternation took place, again followed by 5 days pause upon which the third and final non-cued spontaneous alternation session was performed. Following a 10 days pause the water was removed and for the next 21 days the taste aversion experiment took place. After the taste aversion experiment the animals again received water ad libitum and were given a 26 days pause. Upon this pause followed the cued spontaneous alternation experiment in which the three sessions were distributed like the sessions of the non-cued spontaneous alternation experiment (5 days pause between each session day). Following the cued spontaneous alternation experiment the animals were allowed a 26 days pause during which their body weights were gradually reduced to 80% of the ad libitum values. At the end of this period the extinction experiment was started. After termination of this experiment the animals were allowed free access to food during 160 days. Finally, the rats were food deprived for 24 h and subjected to the exploration experiment.

**FOOD AND WATER INTAKE**

During the food and water intake experiment the animals lived in cages in which the floor was covered with paper only (normally the floor was covered with saw dust). They had ad libitum access to a known amount of water in a bottle offered in the usual position (protruding from the ceiling of the cage) and likewise ad libitum access to a pre-weighed amount of food which was scattered on the floor of the cage. Daily measures were taken of the body weight of the animal, the amount of water and food consumed during the last 24 h, corrected for all food remains (including powdered which were collected and weighed). The daily measures of body weight, water and food intake continued until the animal reached its preoperative body weight. From this experiment the following parameters were registered: the number of postoperative days on which the animal exhibited aphagia (defined as food intake of less than 1.0 g), the number of postoperative days on which the animal exhibited adipsia (defined as a water intake of less than 5.0 ml), the number of days until the body weight of the animal began to increase (as compared to the body weight of the previous day), and the number of days until the animal regained its preoperative weight.

**SPONTANEOUS ALTERNATION - NON-CUED AND CUED**

In each spontaneous alternation session an animal was given two runs. The rat was placed in the start box and immediately released. After entering one of the arms the rat was kept in that arm for 60 s with the aid of a transparent door. Then the animal was transferred to a waiting cage for 15 s. Upon this pause the rat was returned to the start box and im-
mediated. After entering one of the arms the rat was immediately removed from the maze. The only difference between the non-cued and cued spontaneous alternation was the presence or absence of the black and white "cues" (see APPARATUS). From the spontaneous alternation experiment two variables were registered from both the non-cued and cued version of the task: the number of perseverative responses (number of instances on which the response of the second run was to the same side as that of the first run on the same day) and (in order to measure whether the "cueing" changes the animal’s initial left/right preference) the number of first runs on which the left arm was visited.

**CONDITIONED TASTE AVERSION**

For the 21 days of the conditioned taste aversion experiment the animals had access to water only during a 20 min period in the middle of the afternoon. Their water bottles were weighed before and after this period and the daily water consumption was calculated. On days 15, 18 and 21, however, instead of plain water the animals received a 0.1% saccharine sodium solution. Furthermore, on day 15 and 18, 5 min after removal of the saccharine solution the animals received an i.p. injection of 15 ml/kg body weight LiCl (0.12 M solution in water). The consumption of the saccharine solution on the three conditioning days were analysed both as the absolute consumption (measured in ml) and as percentage of the water consumption on the previous day.

**VARIABLE INTERVAL-30 EXTINCTION**

Since the animals had prior experience with operant chambers of the present type, habituation and magazine training were largely unnecessary. On Day 1 they received a combined habituation and magazine training session and on Day 2 they were briefly reshaped. On Day 3 they received a 20 min CRF session and on Day 4 they began training on the variable interval (VI)-schedule which had a gradual increase of the mean intervals: 20 min sessions were given with the following values: Day 4 VI-5, Day 5 VI-10, Day 6 VI-15, Day 7 VI-20, Day 8 VI-25 and Day 9 VI-30. Training on the VI-30 schedule (20 min daily) continued on Day 10 and the following days until the animal had reached the VI-30 training criterion. The demands of this criterion were (1) that the animal had been trained for at least 10 days on VI-30, (2) that the number of bar presses in a certain day must not differ from the numbers on each of the two preceding days by more than 20%, and (3) if demand number 2 was met before the animal had received 15 days of VI-30 training, the number of bar presses recorded on the criterion day should be above 500. After the criterion day the animal started on the VI-30 extinction procedure which lasted the following 5 days. Each VI-30 extinction session was 50 min long: the first 20 min were identical to the previous VI-30 training sessions. During the last 30 min no reinforcement pellets were given, but the pellet machine continued delivering the sound usually associated with pellet delivery at intervals determined by the VI-30 schedule. From this experiment both the number of training days required to reach the VI-30 criterion and the responses on the five extinction days were analysed. From each of the extinction days the following measures were taken: the number of responses during the initial 20 min conditioning period, the number of responses during the 30 min extinction period measured as percentage of the responses during the conditioning period, the number of responses during the first 20 min of the extinction period as percentage of the responses during the conditioning period, and the number of responses during the last 10 min of the extinction period as percentage of the conditioning period.

**VERTICAL HOLE-BOARD EXPLORATION**

Each animal was subjected to only one exploration session during which no explicit reinforcement was given. The rat was placed in the hole-board apparatus, the top was closed, and the experimenter immediately left the room, allowing the animal 15 min of undisturbed exploration. The apparatus automatically recorded all hole-visits, storing the
information about duration and position of the visits. A hole visit would be registered if the animal simultaneously broke both a horizontal and a vertical infrared line, thereby also indicating the position at which the visit occurred. Previous observations indicate that almost all such visits are performed by passing the nose, and in some instances also the mouth, through a hole. The following measures were taken: number of individual visits, total duration of visits, the mean duration of individual visits, and number of different holes visited.

During all behavioural procedures the experimenter was kept ignorant about the group to which an individual rat belonged.

**Surgery**

All animals were anaesthetized with Equithesin (3.3 ml/kg i.p.). The ablations were made by subpial suction with the help of an operating microscope. For details about surgery see Mogensen and Divac (1984). The sham operated control group underwent procedures similar to those of the ablated groups but for the removal of cortical tissue.

**Histology**

Upon termination of all behavioural testing the rats were deeply anaesthetized and transcardially

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**Fig. 1.** The cortical lesions of the four ablated groups: A, Lesion of the ventral prefrontal cortex. B, Lesion of the dorsal part of the anteromedial cortex. C, Lesion of the total anteromedial cortex. D, Lesion of the anterolateral cortex (non-prefrontal control lesion). Black, the tissue removed in all animals. Horizontal stripes, the tissue removed in at least one rat. The diagrams show levels 12.0, 10.5, 9.5, 7.6, and 6.8 mm in front of the interaural line (Paxinos and Watson 1982).
perfused with saline followed by a 10% formalin solution. The brains were removed and allowed to sink in a 10% formalin solution containing 20% sucrose at 4°C. The brains were then rapidly frozen in isopentane cooled to -70°C and cut in a cryostat. The Nissl-stained sections were examined and the lesions were reconstructed with the aid of a microfiche reader.

**RESULTS**

**Anatomy**

The lesions are illustrated in Fig. 1. The neuropathological examination of the brains demonstrated that apart from the cortical ablations (illustrated in Fig. 1) no differences could be established between the experimental groups.

**Behaviour**

**FOOD AND WATER INTAKE**

The results of the food and water intake experiment are shown in Table I. All parameters were subjected to the Kruskal-Wallis analysis of variance (Siegel 1956). Numbers of days on which an animal exhibited aphagia or adipsia were found to show significant group differences at the $P<0.01$ level of confidence while the number of days it took the rats to regain preoperative weight showed group differences significant at the $P<0.05$ level. For group by group comparisons the Mann-Whitney U test (Siegel 1956) was used. For the variable "number of days aphagic" the anterolateral group was found to be impaired at the $P<0.01$ level when compared to both the sham and the total anteromedial groups; the ventral group was different from the sham group at the $P<0.05$ level. The "number of days adipsic" revealed a difference between the ventral and sham group at the $P<0.05$ level, between the ventral and the dorsal anteromedial group at the $P<0.01$ level and between the ventral and total anteromedial at the $P<0.01$ level. For the number of days to regain preoperative weight the ventral group was found to differ from the sham group at the $P<0.05$ level while differing from the total anteromedial group at the $P<0.01$ level. Finally, the dorsal anteromedial group dif-

TABLE I

<table>
<thead>
<tr>
<th>Food and water intake</th>
<th>Median (range)</th>
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<tr>
<td></td>
<td>Sham</td>
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<tr>
<td>Number of days aphagic</td>
<td>0.0</td>
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<tr>
<td></td>
<td>(0–1)</td>
</tr>
<tr>
<td>Number of days adipsic</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>(0–1)</td>
</tr>
<tr>
<td>Number of days to beginning of weight gain</td>
<td>7.5</td>
</tr>
<tr>
<td>Number of days to regain of preoperative weight</td>
<td>18.0</td>
</tr>
</tbody>
</table>

$x$Significantly different from sham ($P<0.05$); $xx$Significantly different from sham ($P<0.01$); $+$Significantly different from total anteromedial ($P<0.05$); $+++$Significantly different from total anteromedial ($P<0.01$); **Significantly different from dorsal anteromedial ($P<0.01$).
fered from the total anteromedial group at the $P<0.05$ level.

**SPONTANEOUS ALTERNATION**

The Kruskal-Wallis analysis of variance (Siegel 1956) of the results of the spontaneous alternation experiment revealed that out of the four measures only the number of perseveratory responses in the cued version of the spontaneous alternation test showed significant group differences ($P<0.05$). The Mann-Whitney $U$ test (Siegel 1956) showed in turn that on this measure the total anteromedial group made a significantly higher number of perseveratory responses (median value: 1.0; range: 1-3) than the sham group (median value: 0.0; range: 0-1) ($P<0.01$) and the ventral group (median value: 0.0; range: 0-2) ($P<0.05$).

**CONDITIONED TASTE AVERSION**

The Kruskal-Wallis analysis of variance (Siegel 1956) of the results of the conditioned taste aversion experiment revealed that none of the measures from the second and third conditioning days (on which the actual conditioned taste aversion could be measured) nor the measures from the first conditioning day (on which group differences in the non-conditioned responses to the saccharine solution might have appeared) showed any significant group differences.

**VARIABLE INTERVAL-30 EXTINCTION**

The Kruskal-Wallis analysis of variance (Siegel 1956) of the results of the VI-30 extinction experiment revealed that none of the measures of this experiment contained significant group differences.

**VERTICAL HOLE-BOARD EXPLORATION**

The results of the vertical hole-board exploration experiment are shown in Table II. Kruskal-Wallis analysis of variance (Siegel 1956) revealed that significant group differences were present in the measure "mean duration of visits" ($P<0.01$). The Mann-Whitney $U$ test (Siegel 1956) revealed that "the mean duration of visits" for the ventral group was significantly longer ($P<0.01$) than the corresponding values for all other groups.

<table>
<thead>
<tr>
<th>Vertical hole-board exploration</th>
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<tbody>
<tr>
<td><strong>Median (range)</strong></td>
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</tr>
<tr>
<td></td>
<td>Sham</td>
</tr>
<tr>
<td>Number of individual visits</td>
<td>42.5 (13–61)</td>
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<tr>
<td>Total duration of visits (s)</td>
<td>81.5 (18–114)</td>
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<tr>
<td>Mean duration of individual</td>
<td>1.82 (1.38–2.22)</td>
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<tr>
<td>visits (s)</td>
<td>Number of different holes visited</td>
</tr>
</tbody>
</table>

***Significantly different from sham ($P<0.01$); **Significantly different from total anteromedial ($P<0.01$); **Significantly different from dorsal anteromedial ($P<0.01$); **Significantly different from anterolateral ($P<0.01$).
DISCUSSION

Impairments of intake of food or water, or both, were observed only in two groups. The animals with lesions of the ventral PFC were both aphagic and adipsic while the anterolateral lesions induced only aphagia. Both groups resumed eating and drinking soon after surgery and no force-feeding was necessary. Since the complete mesial lesion did not influence food and water intake, adipsia and aphagia in the ventral group should be attributed to the lesion of the lateral portion of the ventral cortex. Such a finding is in agreement with the results of Kolb (1974a), Kolb and Nonneman (1975) and Kolb et al. (1977). Our results show, however, that the large anterolateral frontal lesions of previous studies included two relevant areas, the suprarhinal cortex and the anterolateral (non- prefrontal) cortex. Each of these areas appears to affect food and water intake differentially. It could be speculated that while the suprarhinal cortex might primarily be involved in motivational aspects of food and water intake, the impairments observed after lateral lesions are rather a consequence of sensory-motor disturbances.

In the non-cued spontaneous alternation task no impairment was seen in any group. In the cued version, however, a slight but significant impairment was found in the total anteromedial group. In the latter version of the task the dorsal anteromedial group made more perseverative responses than the sham and the ventral PFC groups, but these differences did not reach significance. Possibly, in some earlier studies (e.g. Divac et al. 1975b) a differential cue was not noticed by experimenters but was available to the animals. In neither the non-cued nor the cued spontaneous alternation task did the groups differ on their first choice response tendencies. Obviously, further research is needed to provide a better understanding of the present observations. Presently, however, it appears reasonable to conclude that while the anteromedial cortex is significantly involved in mediation of the cued spontaneous alternation task, the absence of salient visual cues changes the task in such a way that anteromedial cortical participation is no longer essential for mediation of the task solution.

The results of the conditioned taste aversion experiment show that ablation of the rat equivalent of the entire orbital cortex fails to induce impaired solution of this task. All groups, including those similar to the groups of a previous study (Divac et al. 1975a) behaved like the sham operated controls. Such results clearly speak against the hypothesis that lesions of the prefrontal cortex produce "interoceptive agnosia" (Nauta 1971). It may be noted that a number of other studies (review in Ivanova and Bures 1990) have found conditioned taste aversion to be unaffected by various cortical as well as subcortical lesions in the rat.

None of the presently studied groups was impaired in extinction of food rewarded bar pressing. This result was obtained in spite of our efforts to replicate the task and orbital prefrontal lesions used in similar experiments on monkeys (Butter et al. 1963, Butter 1969). The present results are in agreement with other reports as far as the anteromedial prefrontal cortex of the rat is concerned (Schwartzbaum et al. 1964, Kolb et al. 1974, Nonneman et al. 1974, Mogensen and Divac 1984). However, there is less than perfect agreement on the role played by the suprarhinal cortex: while the presently observed lack of impairment agrees with the results of Nonneman et al. (1974) and Mogensen and Divac (1984), Kolb et al. (1974) found impaired extinction after suprarhinal lesions. It might be of interest in the future to study more directly whether the potential involvement of the suprarhinal cortex in mediation of extinction is highly dependent on the apparatus and procedures employed during behavioural testing (compare to results reported by Geoffroy and Mogensen (1988) and Mogensen et al. (1987)). One can tentatively conclude that the orbital areas of monkeys and rats differ in the degree to which they are involved in extinction of operantly conditioned responses. Consequently, in the rat it is hard to interpret the symptoms of prefrontal cortical lesions as reflections of "disinhibition" (Brutkowski 1965).

The only parameter of the vertical hole-board exploration test which revealed significant group diff-
ferences was the mean duration of the individual hole visits. In this parameter the animals subjected to ablation of the ventral prefrontal cortex revealed a significantly longer mean visit duration compared to any other group. This behavioural change may be a consequence of ablation of the lateral part of the ventral region (including the suprarhinal area) since the mesial part of the ventral region (as part of the total anteromedial cortex) was lesioned without significant effects on the vertical hole-board exploration. The ability of the vertical hole-board test to reflect in a sensitive manner the ways in which exploration is modified by neural manipulations has been demonstrated in a series of studies utilizing a broad spectrum of neural manipulations (e.g. Iversen and Mogensen 1984, 1988, Geoffroy and Mogensen 1988).

In a study allowing rats the opportunity to investigate a single hole (located in one of the walls of a test box) Kolb (1974b) found in the first session that visit time to this hole was unaffected by lesions of either the total anteromedial cortex or the suprarhinal prefrontal region. Comparisons across various measures of "exploration" and "locomotion" can, however, be misleading (e.g. Weasner et al. 1960, Geoffroy and Mogensen 1988). Furthermore, it should be noted that exploration tests such as the vertical hole-board test of the present study include no explicit reinforcement of the animal's responses. Therefore, comparisons of the outcome of the present hole-board test to the results of hole-board based place learning studies (e.g. Kesner et al. 1989) are complicated by the different nature of the tasks (exploration versus place learning) and should be discouraged.

A substantial part of the exploration performed in the vertical hole-board exploration test - at least such exploration that reflects itself in hole visits - is likely to be dominated by processing of olfactory cues. Electrophysiological (e.g. Clugnet and Price 1986) as well as behavioural (e.g. Eichenbaum et al. 1983) experiments indicate that the suprarhinal rather than anteromedial prefrontal cortex is closely associated with olfactory functions. Olfactory processing in the suprarhinal region may contribute to the present observation of a rather selective involvement of the lateral part of the ventral prefrontal cortex in vertical hole-board exploration.

In conclusion, the present study has demonstrated consequences of lesions within the prefrontal cortex of the rat in three behavioural situations: the regulation of food and water intake, the exploration of a vertical hole-board (both changed after ablations of the ventral prefrontal cortex), and cued spontaneous alternation (changed after ablation of the total anteromedial cortex). Both regulation of food and water intake and hole-board exploration were most likely influenced by lesions within the lateral part of the ventral cortex (including the suprarhinal cortex) whereas the cued spontaneous alternation was affected by lesions of the anteromedial cortex. These results demonstrate a double dissociation which in addition to earlier observations (review in Kolb 1984) support the notion that even in the rat the prefrontal cortex is functionally heterogeneous.

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