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Behavioural Brain Research 117 (2000) 173–183

BEHAVIOURAL BRAIN RESEARCH

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Research report

Lesions of the medial shell of the nucleus accumbens impair rats in finding larger rewards, but spare reward-seeking behavior

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Received 25 April 2000; received in revised form 25 July 2000; accepted 25 July 2000

Abstract

The goal of this study was to help better understand the importance of the nucleus accumbens (Nacc) in the processing of position and reward value information for goal-directed orientation behaviors. Sixteen male Long–Evans rats, under partial water deprivation, were trained in a plus-maze to find water rewards in the respective arms which were lit in pseudo-random sequence (training trials). Each day one reward arm was selected to deliver six drops of water (at 1 s intervals) the others provided only one drop per visit. After 32 visits, probe trials were intermittently presented among training trials. Here, all four arms were lit and offered the previously assigned reward. The rats rapidly learned to go to the highly rewarded arm. Six trained rats were given bilateral electrolytic lesions in the Nacc shell, two others had unilateral lesions and eight had sham operations (with approved protocols). Field potentials evoked by fornix stimulation were recorded in lesion electrodes to guide placements. Only the lesioned rats showed significant impairments ($P < 0.05$) in selecting the greater reward on probe trials. However on training trials, lesioned (and sham-operated) rats made only rare errors. While the motivation to drink and the capacity for cue-guided goal-directed orientation behavior was spared, lesioned rats were impaired in learning the location of the larger reward. The accumbens lesions apparently impaired integration of position and reward value information, consistent with anatomical and electrophysiological data showing the convergence of hippocampal, amygdalar, ventral tegmental area (VTA) and prefrontal cortical inputs there.

Keywords: Ventral striatum; Motivation; Hippocampus; Amygdala; Spatial learning; Navigation

1. Introduction

Both anatomical [5,8,9,11] and neurophysiological data [12,16,17,23] indicate that the shell region of the nucleus accumbens (Nacc) is a site of integration of spatial (from ventral hippocampal CA1/subiculum) and reward information (from ventral tegmental area, that is, VTA, as well as amygdala). This convergence of afferents in the Nacc could provide the principal information required to accurately navigate in space, namely the relation between the present location of the animal, the environmental cues, the motivation to go to (or avoid) other locations and reward availability. Furthermore since the major projection areas of the Nacc consist of various motor, effector and activating regions such as the ventral pallidum, pedunculopontine nucleus, hypothalamus, substantia nigra and VTA, this suggests that the Nacc is involved in the initiation of goal directed behaviour.

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0166-4328/00/$ - see front matter
PII: S0166-4328(00)00303-X

However behavioral studies have revealed conflicting results following lesions of the Nacc. Electrolytic and neurochemical lesions of the Nacc induce impairments in alternation and reversal learning in the T-maze [2,24] and learning of a win/shift version of an eight-arm radial maze [22]. However Floresco, et al. [7] and Schacter, et al. [21] found no such impairments. Other studies have employed the T-maze that has been challenged as to whether it tests for spatial learning, or simply motor responses. In this task both Annett et al. [2] and Taghzouti et al. [24] concluded that the impairments demonstrated following Nacc lesions had no relation to spatial localization capacities in their rats.

Deficits in acquisition of the water maze task (with the submerged escape platform) are caused by Nacc lesions with ibotenic acid or intraccumbens haloperidol injections [20], but not by 6-OHDA dopamine depletion in Nacc and prefrontal cortex [10] or intra-accumbens lidocaine injections [7]. However the lesioned animals do eventually succeed at locating the platform [2]. This suggests that other brain systems can be involved in learning this task, albeit more slowly, perhaps by habit learning or simple guidance strategies rather than the use of configurational cues or 'mapping'. Thus successful performance in this task, at least with the analyses and criteria used by the latter authors, is possible with brain structures other than Nacc, and in this respect the water maze task lacks specificity.

In an attempt to surmount these difficulties in studying the specific role of the Nacc shell in orientation and displacement behaviors, we have developped a new behavioral task requiring rats on a daily basis to learn which maze arm is currently providing the largest rewards. Daily changes in the location of the largest reward prevents habit-learning from being employed successfully. Rather, the task permits analyses to discriminate several different types of strategies (motor response, place preference, or actual acquisition of a position-reward association). It also has low working memory demands. In addition, the frequent cue-guided trials provide a control for the level of motivation.

Possible reasons for the equivocal results concerning the role of Nacc (shell and core regions) in spatial behavior may be related to lesion-making methodology. Difficulties may arise from the fact that some studies include uncontrolled combinations of lesions to the shell and core regions of the Nacc, each of which have different anatomical connectivity and neurochemical properties. But even more anatomically selective lesions of the Nacc shell by micro-injections of lidocaine [22] or kynurenic acid (a glutamate antagonist) [21] have led to different results in rats performing the same win/shift version of the eight-arm radial maze. Perhaps this is caused by anatomical constraints: the thin Nacc shell extends along the medial and ventral surface of the Nacc core for its entire rostro-caudal extent. Small single injections might have inactivated different fractions of the Nacc shell, and risked nonetheless to have spread to the adjacent core. Furthermore fibres of passage would continue to innervate the spared portions of the Nacc shell.

Here we selected the electrolytic lesion technique. This permitted electrode placements under guidance of field potentials evoked by fornix stimulation. In this way, its position in the hippocampal projection zone could be directly verified. In addition, a massive destruction of afferent fibers from hippocampus was desirable since the shell region of nucleus accumbens is too widespread and narrow to conveniently permit a comprehensive but restricted series of microlesions. Since anatomical studies have shown that the hippocampal and amygdalar inputs to the nucleus accumbens enter through the dorsal part of the medial shell, medial to the anterior commissure [8], we directed lesions to this zone. Thus while no lesions were made to the ventral shell, the anatomical data indicate that these electrolytic lesions also likely interrupted its afferents from amygdala and hippocampus. Some of these results have previously been presented in abstract form [1].

2. Material and methods

2.1. Experimental animals

Sixteen male Long–Evans rats (320–350 g; CERJ, Le Genest-St-Isle, France) were water deprived during weekdays and maintained at not less than 85% body weight. Food was provided ad libitum. Animals were weighed and examined daily. In training and recording sessions the rats were permitted to acquire water until satiation, then supplemental water was provided as necessary to maintain body weight. Rats were permitted to rehydrate completely prior to weekends. All animal experimental protocols as well as housing conditions were in strict adherence with institutional, national and international standards and regulations. The animals were maintained in an animal care facility with lighting on a 12 h on/12 h off cycle.

2.2. Behavioral task and experimental design

In a square black curtained enclosure (3×3 m, see Fig. 1), a white poster board (180×60 cm) was mounted on the wall opposite the entrance. The poster board was lit up during training and experiments and served as the principal environmental cue. The experimenters and all equipment were outside the curtains. An elevated black platform (180 cm diameter) was situated at the center of the enclosure. Barriers in the form of outwardly inclined wall inserts (25 cm high) were positioned on the platform to form a plus maze

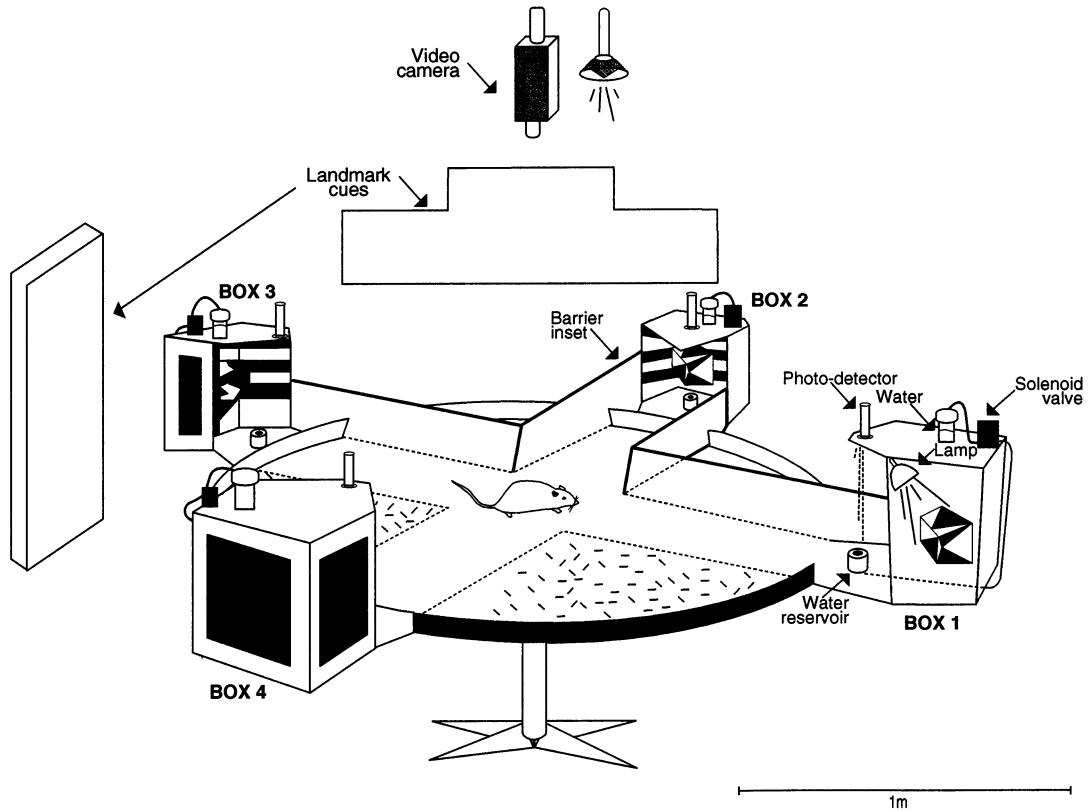

Fig. 1. The experimental plus maze was bordered by inclined walls and had four identical reward boxes. In the automated task under computer control, drops of water were delivered from water reservoirs through the respective solenoid valves when the rat blocked the photodetectors. There were two principal landmark cues on the walls outside the maze to aid the rat in orienting in the experimental environment.

with 30 cm wide arms. At the end of each arm were identical alcoves ('reward boxes'; $30 \times 30 \times 30$ cm). In each box, near the edge of the platform, was a short cylinder with a slight recess at the center of the top surface. A hole drilled from the bottom of this recess to the bottom of the cylinder transmitted water rewards which arrived via tubing connected to a solenoid valve and an elevated reservoir. Mounted in the back of the reward box was a highly contrasted, mobile polyhedron that served as a visual cue. The cues were identical in each reward box and could be illuminated independently under computer control. Delivery of water rewards in the respective boxes was automatically triggered after the rat arrived and tripped a photobeam mounted above the water reservoir.

2.3. The behavioral task (Fig. 2)

During training trials, reward boxes were illuminated one by one and water rewards were only available at the lit box. When the rat arrived at the center a photodetector automatically triggered the light to go on at the next reward box. There was no signal for error trials other than withholding water, and the box remained lit until the rat arrived there. The reward boxes were lit in a pseudo-random sequence that never pro-

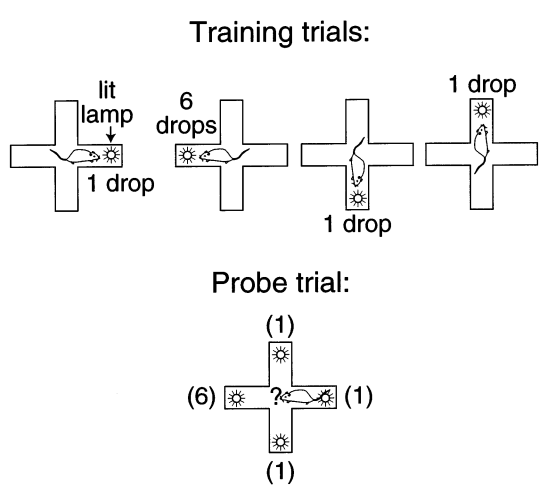

Fig. 2. The behavioral task. The rats were trained to get water rewards at the lit box (training trials). The boxes were lit in a random sequence. When the rat arrived at the center an automated system triggered the next light, and arrival at the lit box triggered the water reward. Each day a different box was selected to deliver six drops of water while the others delivered only one drop. After 32 visits, probe trials were intermittently presented: all four boxes were lit and armed. Although all boxes provided their ration of water on probe trials, the rats rapidly learned to go to the box delivering six drops of water.

vided more than two successive rewards at the same arm and also avoided requiring more than two successive repetitions of the same type of re-orienting movement upon returning to the maze center (turning left, right or by 180°, going straight ahead). Each day one of the alcoves was selected to deliver six drops of water at 1 s intervals while the others delivered only one drop (calibrated at 30 μl). When the rat arrived at this reward box, this triggered the delivery of the appropriate amount of water. After 32 training trial visits (including eight visits to the arm dispensing six drops of water), probe trials were presented at irregular intervals among the training trials. For probe trials all reward boxes were lit and enabled to deliver their assigned volume of water. Although on probe trials visits to any of the boxes successfully triggered water delivery, the rats rapidly learned to go to the box delivering six drops of water. Since this was the default behavior of all rats, visits to maze arms providing only one drop of water during probe trials will, for brevity, be referred to as 'error trials'. The timing of the blocking and unblocking of the photobeams as well as opening of solenoid valves were all coordinated by our own software (based on programs written by Dr O. Trullier), and executed and recorded by the DataWave data acquisition system (Longmont, CO, USA).

2.4. Performance measures

In each session at least ten probe trials were run, and the score was calculated as the percent of these trials performed correctly. Each rat was tested for 5 successive days prior to surgery, and five more after recovery from surgery. An analysis of variance examined repeated measures in the lesion and sham groups. Pairwise *t*-tests compared the pre-surgery and post-surgery scores measured for each animal. Analyses of response bias in error trials were conducted using the chi-square test. Statistical tests were performed with Statistica® (Tulsa, OK) or Microsoft® Excel.

Testing began about 1 week after the surgery and was repeated on 5 consecutive days. Rats in the lesion group were tested for 2 or 3 additional (and consecutive) days to allow for the possibility of slower relearning of the task. In these cases only data from the final 5 days of testing were analyzed statistically (to assure equal numbers of measures for the pair-wise *t*-tests).

2.5. Lesion surgery

After reaching plateau levels of performance, eight rats were operated surgically to make electrolytic lesions of the Nacc while eight others had sham lesion operations. Rats were returned to ad libatum water for at least 2 days prior to surgery. First they were tranquilized with 0.1 ml xylazine (Rompun®) intramuscularly then anesthetised with 40 mg/kg pentobarbital. The Nacc lesion electrode placement was made by recording from it field potentials evoked by hippocampal stimulation. A pair of 60 μm diameter insulated stainless steel stimulating electrodes separated by one mm were placed in the fornix/fimbria (AP −1.3 mm, ML 0.9 and 1.9 mm). The final depth of the placement of the stimulation electrodes was 3.7 mm, but they were first lowered to 4.0 mm, then raised to overcome possible indentation of the surface without penetration. The lesion electrode (an etched 200 μm acupuncture needle treated with insulating varnish) was placed ipsilaterally under stereotaxic control at AP 1.4 mm, ML 0.7 mm. Stimulus volleys (0.2 μs, bipolar, 0.4–0.6 mA) were delivered to the ipsilateral fornix via the bipolar electrodes. Signals in the lesion electrode were filtered (300–5000 Hz) and amplified with an A-M Systems model 1800 differential amplifier. Data were acquired on a PC hard disk with a Cambridge Electronic Design 1401 data acquisition system (Cambridge, UK) employing their SIGAVG® program which sampled at 5 kHz averaged over 16 stimuli with at least 7 s intervals between each pulse. Positive field potentials at delays 8 and 20 ms (characteristic of the fornix to accumbens pathway [3]) were searched for in recordings at 0.5 mm intervals at depths ranging from 4.5–8 mm (see Fig. 3). Two or three electrolytic lesions (typically 100 μAmp cathodal current for 20 s) were applied at points separated by 0.6–1.0 mm centered within this zone. Lesions were made only along one electrode track starting ventrally then progressing dorsally. If no satisfactory field potentials were evoked along the electrode track, responses were tested at a different electrode placement. Control animals were also operated using the same procedures except that (for six of the eight) only the stimulating electrode was implanted, and the same stimulation was applied 50 times, again respecting the minimum 7 s interval between successive pulse trains. The stimulation procedure was repeated on left and right sides in lesion and sham operated animals. The scalp was closed with suture and treated with Betadine®. The other two sham operated animals only had scalp incisions while under anesthesia.

2.6. Histology

At the end of the experiments, the rats were given full access to food and water. An overdose of pentobarbital was followed by transcardial perfusion with phosphate buffered saline followed by 4% formaldehyde solution in phosphate buffer. Histological sections were cut on a freezing microtome and stained with cresyl violet. The extent of the lesion site was identified as the zone with no remaining neurons.

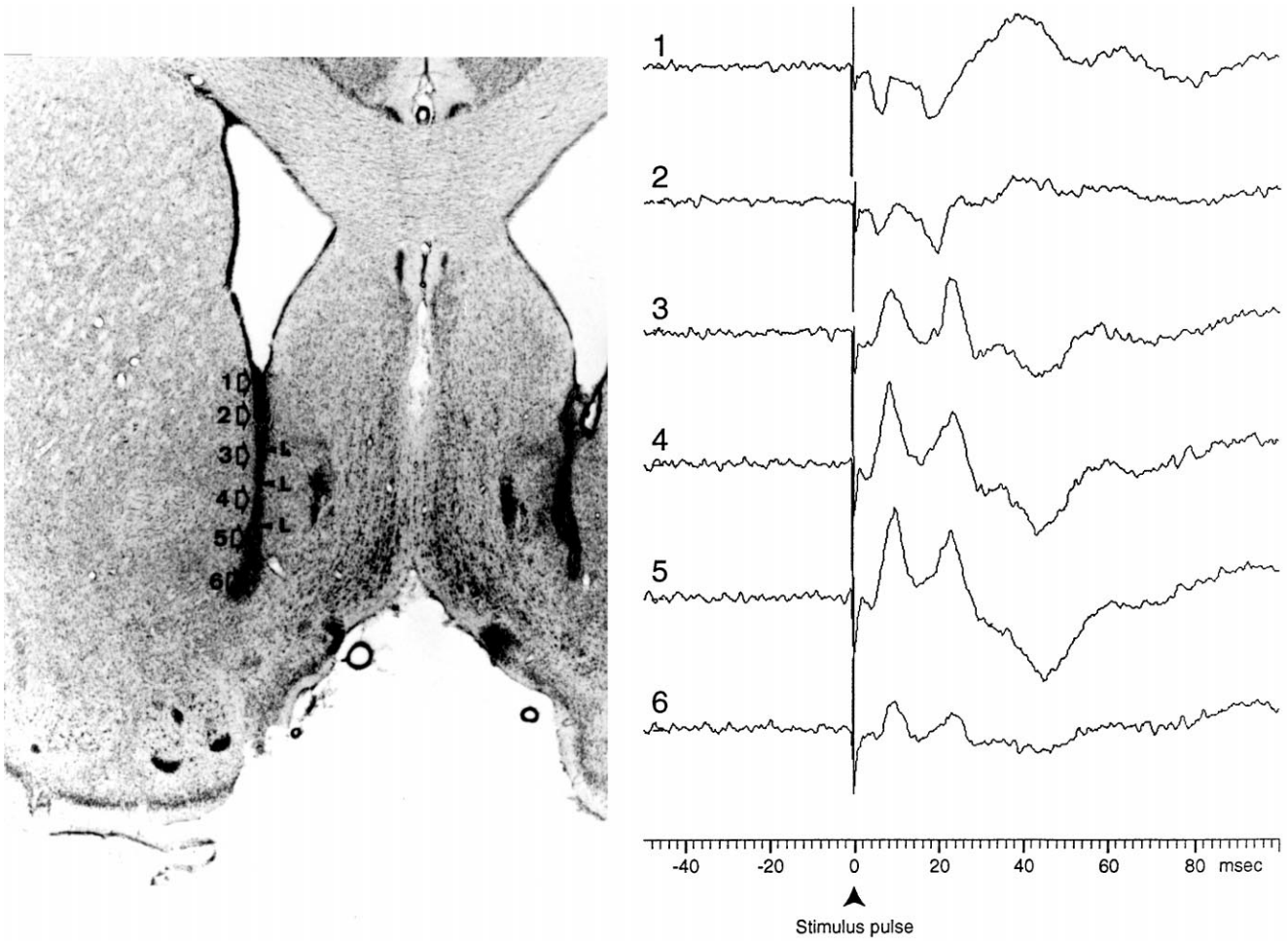

Fig. 3. To the left are the sites of electrolytic lesions. The placements were guided by field potentials evoked by fornix stimulation. Numbers correspond to recording sites; these are 0.5 mm apart. The evoked potentials for the respective sites 1-6 are shown to the right. The sites indicated 'L' correspond to where current was applied through the electrode. (Rat 2-1)

3. Results

The stereotaxic placement of the lesion electrode was confirmed by recording the characteristic positive potentials at latencies of 8 and 20 ms that were evoked by electrical stimulation of the fornix. Fig. 3 shows an example of the reconstruction of the lesion sites and the corresponding field potentials evoked in an electrode track in one of the rats. This corresponds to the coronal plane 1.0 mm anterior to bregma [19]. Recording sites 3, 4 and 5 show the prominent evoked potentials (averaged over ten sweeps), while responses were weaker at position 6. Note that the lesion extends deeper than the site of application of current.

The extent of the damage in each of the lesioned rats is shown in Fig. 4. In the lesion group, cell death in the Nacc was in general restricted to the medial shell region, rarely extended to the ventral shell and never spanned the entire rostro-caudal extent of the shell. In isolated cases damage extended to ventral pallidum, interstitial nucleus of Cajal, islands of Calleja, lateral septum, medial septum, nucleus of the vertical limb of the diagonal band, olfactory tubercle, anterior commissure as well as the medial part of the Nacc core. Usually lesions were in the form of vertically oriented cylinders of diameter 200–300 μm. Rats 2–2 and 2–3 had only unilateral lesions. Rat 1–5 had only a unilateral lesion in a zone medial to the Nacc shell and was excluded from further analysis. Rat 2–6 also had a lesion in the latter zone as well as a well-placed lesion along the medial shell/core border contralaterally — it was retained for analyses. Damage to the fornix (from stimulation electrodes) ranged from minor (track of electrode entry) to negligeable in control and lesion groups (not shown).

Rats were weighed each day. The average weight was computed for each animal for the weeks of pre-operation and post-operation testing. During both of these periods the rats were under water deprivation schedules. The overall average increase in weight was 6.6% for the sham lesion group and 3.0% for the Nacc lesion group. A *t*-test failed to show a significant difference

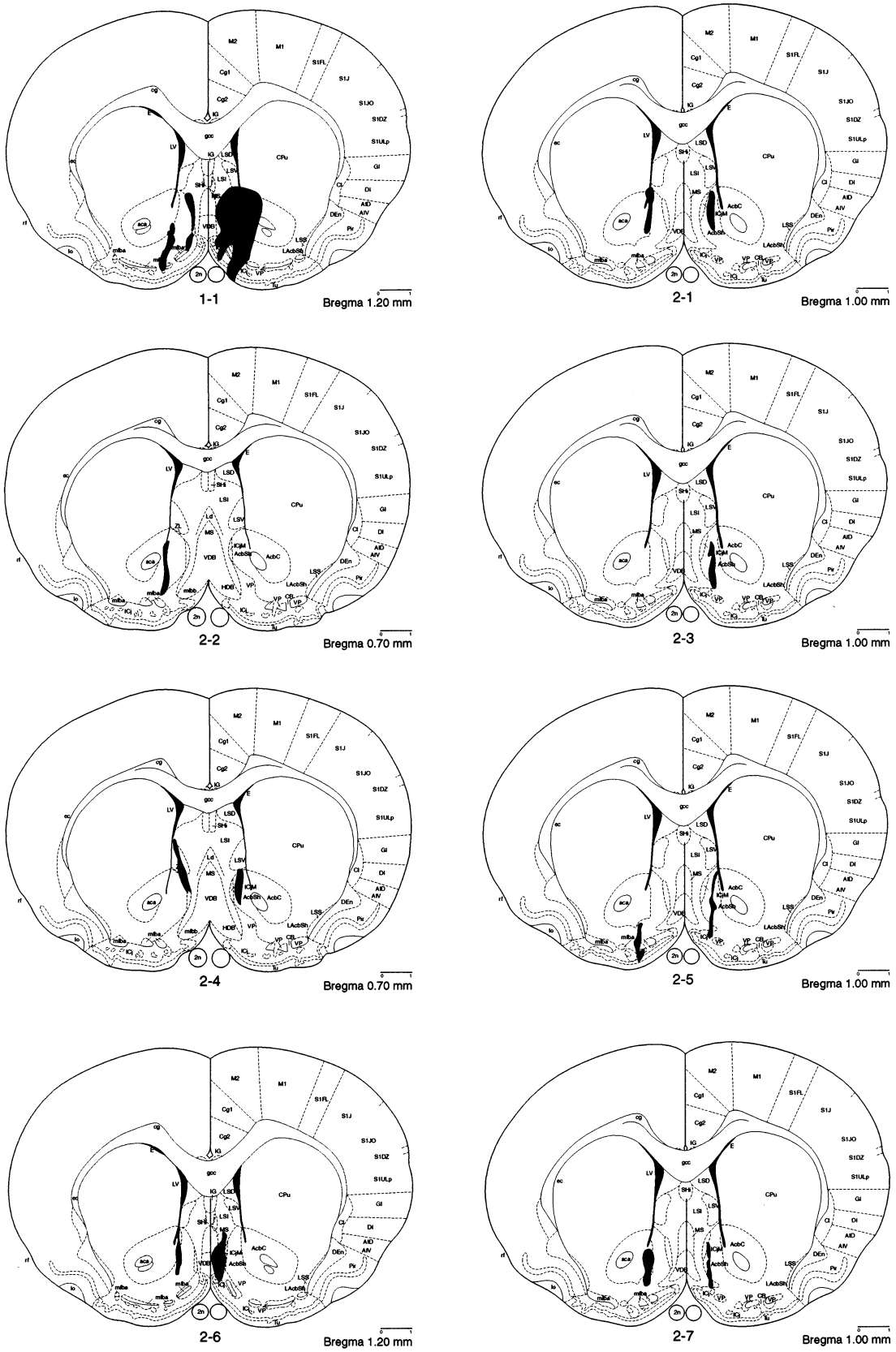

Fig. 4. The section with the maximal extent of the lesions in the coronal plane for each of the rats in the lesion group are indicated by the solid black regions ventral to the lateral ventricles. In general, the lesions were vertically oriented cylinders 200 to 300 μm in diameter. The numbers below each tracing identify the animal. The tracings of the lesions have been superimposed upon figures have been adapted from Paxinos and Watson [19] with permission. Scale bars are 1 mm.

between the weight increases of the two groups ($P = 0.072$).

3.1. Behavioral performance during recording sessions.

Rats of both groups performed almost perfectly on the (light-cued) training trials both prior to and after surgery. The repeated-measures analysis of variance showed significant differences between lesion and sham groups ($F(1, 14) = 21.78$, $P < 0.0004$), between pre- and post-surgery ($F(1, 14) = 498.06$, $P < < 0.0001$) as well as the interaction between these two factors ($F(1, 14) = 316.61$, $P < < 0.0001$). The overall mean score in the sham group diminished only slightly, from $77.3 \pm 2.4\%$ (SEM) prior to surgery to $73.0 \pm 2.9\%$ afterwards (t-test $P = 0.307$; Fig. 5). However in the lesion group the performance average on probe trials plummeted to $40.9 \pm 1.4\%$, from initial levels of $79.0 \pm 2.0\%$ (t-test $P < < 0.0001$). Furthermore dependent t-tests compared, for each individual rat, data measured in the respective weeks prior to and after recovery from surgery (Table 1). Each rat in the lesion group showed significant decreases in performance after surgery while no difference was observed in any of the sham lesioned rats. Even after 1 week of retraining, the best single session performance in the lesion group was 55%. Sham operated controls showed no significant differences in the level of accuracy as compared with pre-operation testing. There were no clear tendencies for performance improvement (or deterioration) over the course of the week of testing in either group. Thus in the group analyses above, the results were averaged for each rat for the pre- and post-surgery periods, respectively.

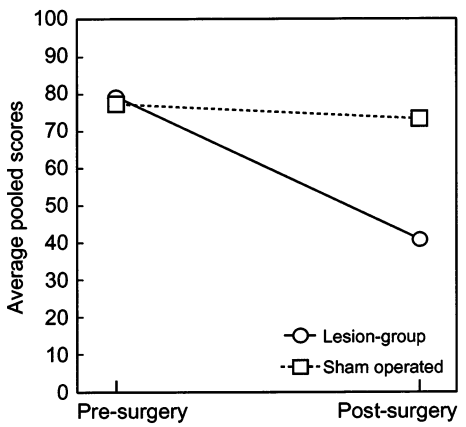

Fig. 5. Performance prior to and after surgery in the sham and lesion groups. Each rat was tested for 5 days prior to and after surgery. The weekly averages for each rat were then pooled for the respective groups.

Table 1
Comparisons of performance prior to and after surgery

	Mean % correct		t-test
Rat	Pre-surgery	Post-surgery	P values
Accumbens medial shell lesion			
2–1	68.6	37.2	0.0135
2–2	77.0	40.8	0.0021
2–3	81.6	45.6	0.0013
2–4	87.6	44.4	0.0000
2–5	79.0	35.0	0.0026
2–6	83.2	43.8	0.0001
2–7	82.2	43.8	0.0072
1–1	72.5	36.7	0.0051
Sham lesion			
3–1	73.8	65.7	0.4753
3–2	64.5	62.8	0.8149
3–3	78.5	77.2	0.8763
3–4	81.0	75.8	0.3893
3–5	78.5	69.3	0.3329
3–6	71.5	65.2	0.1056
1–2	82.5	80.0	0.7650
1–4	88.3	88.3	1.0000

In order to determine whether the errors made by the lesioned rats were random, or rather involved some types of stereotypy, further analyses were performed on their data. The errors on probe trials were analysed to test for two types of perseverance: place preferences or motor responses (turning left, right or going straight or turning 180° at the center). First the errors were examined to determine if the rats showed preferences for particular maze arms (see Table 2). The χ^2 statistic tested whether visits to maze arms on the error trials were disproportionately distributed. In analyses of data pooled from the 5 days of post-operative testing, four of the rats (1–1, 2–1, 2–3, 2–5) showed significant bias in error probe trials, that is, the rats tended to go to certain maze arms more than others (χ^2 test, $P < 0.05$). In analyses of the individual post-operative sessions for each of the eight lesioned rats (five sessions each), in the 'error' probe trials, visits were disproportionately distributed among the boxes in 13 (32%) of the sessions (χ^2 tests; $P < 0.05$). In rats 2–3 and 2–5 this preference for certain maze arms occurred in three of the five sessions, and in two of five sessions in rats 2–1 and 2–4. In all of these sessions, and three sessions in other rats with significant bias in cup selection, the majority of the error choices were for only two of the four maze arms (those opposite the wall with the large visual cue, in the foreground of Fig. 1). However the identities of the preferred arms varied from day to day and among the animals. In seven of the 13 sessions with visits unequally distributed among the low reward arms, a preferred arm was the highly rewarded arm of the previous day, despite the fact that performance on the previous day had been poor (40% correct) in all cases. In six of these seven sessions the preferred, rewarded arms of the previous day were those oriented toward the curtain opposite the large cue. (This curtain separated the experimenters and instrumentation from the

Table 2
Summary of error types in Nacb lesioned rats over 5 days of testing

Maze arms visited during error trials						Preferred re-orientation directions					
Rat number	Arm 1	Arm 2	Arm 3	Arm 4	P value of χ^2	Straight	Left	Right	reverse	P value of χ^2	Sum
1–1	3[a]	13	4	13	0.035	11	14	5	3	0.023	33
2–1	23	10	2[a]	11	0.001	10	8	15	13	0.471	44
2–2	18	12	6[a]	19	0.187	20	25	7	3	0.000	55
2–3	15	4	7	20[a]	0.000	10	13	13	10	0.854	26
2–4	19	13	4[a]	16	0.101	18	8	18	8	0.052	48
2–5	16[a]	6	4	25	0.000	14	21	9	7	0.027	35
2–6	13	8[a]	10	19	0.290	24	14	10	2	0.000	42
2–7	9	19	10	13[a]	0.136	13	30	2	6	0.000	38

[a] This arm was the correct choice on 2 testing days while the others were correct only once. Fewer errors would be expected here.

experimental apparatus.) Thus these error types are partially confounded: the tendencies toward errors at these reward boxes might be related to latent or implicit learning of the reward distribution of the previous day, perhaps in association with some other factors concerning these maze arms. Nonetheless these animals maintained a clear capacity for place preferences. In contrast the same analyses of error trials in the sham lesioned rats showed no significant preference for particular reward boxes or for the box most highly rewarded in the previous session. However the small number of errors in this group may have obscured possible minor tendencies for place preferences.

Secondly, the error trials were studied with respect to the movement that the rat made at the center when re-orienting from the previously visited arm toward the (incorrect) arm providing only one drop of water. This compared the incidence of left turns, right turns, proceeding forward or going in reverse, assuming that these would be equally distributed among the low reward arms. The analyses showed that the re-orienting movements of the rats at the maze center were not equally distributed on error trials in 30% of the sessions. These same sessions only rarely (two out of 40) also showed disproportionate distributions of error visits to particular maze arms in the analyses of the preceding paragraph. In order to determine whether individual rats tended to turn in a particular direction (or go straight ahead) during error trials, the total number of incidences of each type of movement was accumulated for the 5 day testing period (Table 2). χ^2 analyses of these data showed significantly disproportionate distributions of these orientation movements in error probe trials in rats 1–1, 2–2, 2–5, 2–6 and 2–7. In four of these rats, during error trials there were from 2.5 to 15 times fewer turns by 90° to the right (and straight ahead) than to the left, and few 180° turns. In rat 2–4, the result of the χ^2 test missed significance ($P = 0.052$) but there were over twice as many errors involving turning to the right and straight ahead as there were for turning 90° to the left as well as by 180°. The two rats with unilateral lesions showed performance levels and error patterns indistinguishable from those of bilaterally lesioned animals, an observation to be replicated with a larger data set. All but two of the sham lesioned rats also showed significant preferences for certain movement types in their error trials. Interestingly, in all of the latter rats with sufficient data, most errors also involved left turns at the choice point, while 180° turns were least common.

Note that in the analyses of data pooled over all post-operative trials, lesioned rats 1–1 and 2–5 both had significant arm preferences and re-orientation preferences during error trials. These two effects do not appear to be confounded (for example, left turns and visits to cup 1 always occurring together on error trials). In the error analyses of individual sessions from these two rats, only one (of ten) showed significance for both types of bias (χ^2 test). The remaining rats showed either arm preferences or dominant re-orientation movements within a given session. These data indicate that arm preference and movement preference were alternate and unrelated strategies.

4. Discussion

The principal findings of this study are that electrolytic lesions of the medial shell of the Nacc impair learning to go to the maze arm providing the largest rewards, but preserve reward-seeking behaviour that is guided by a visual cue. The latter result, and the fact that the weights of the lesioned animals remained normal, confirms that they were capable of being motivated to execute orienting behaviours toward reward sites [13,22]. Thus the failure in probe trials to seek out the greatest reward was not due to a lack of motivation. In the first part of each session when only training trials were presented, the rats had at least eight trials at the arm providing the largest reward. There rats always

remained until the sixth drop of water was delivered and the cue light was turned off. This and the fact that the six water drops were distributed at 1 s intervals provided the rats ample opportunities to register that greater quantities of water were being given there. In addition, the probe trials were presented intermittently among cue-guided training trials that continued to include visits to the arm providing large rewards.

In the animals with accumbens lesions, reward box choices did not become completely random. Rather, most of the rats tended to show preferred error types, albeit not in a completely consistent manner over all sessions. Two strategies were detected: repeated visits to certain arms, and repetition of the same turning (or continuing straight ahead) responses at the maze center. Both of these could be considered as examples of types of perseverative or habit-like behaviors that have been shown to be preserved after lesions of the hippocampal system. The lesioned rats did show a tendency to visit certain arms more than others in probe trials in 30% of the sessions. This shows that these rats were able to distinguish, to some degree, among the respective arms. However preferences were for two among the four maze arms, indicating more a generalized taxis-like response in relation to cues rather than a precise map-like representation or accurate utilisation of cue configurations in these accumbens lesioned animals. While the rats were able to discriminate cues distinguishing the maze arms, there was an impairment in the ability to associate these cues with the position of the highly rewarded arm or the movements necessary to orient towards it.

A particularly intriguing observation was that the preferred maze arms during error trials often corresponded to the arm providing the large reward on the previous day. This was surprising since performance on the previous day was poor in comparison with pre-operation scores. This suggests that the rats might have been gradually acquiring information on the previous day that they were unable to express until the following day, when the information was no longer valid. If this can be confirmed, it would be consistent with the notion that, in the case of dysfunction in the hippocampal-accumbens system, alternate pathways such as dorsal striatum [6,14,18] persist in mediating other types of learning. However the delay in acquiring the previous day's correct response observed here indicates that the time course of these types of learning is slower, and in our paradigm the daily change in the highly rewarded location foiled their effectiveness. While rats with accumbens lesions have slower acquisition in the Morris water maze (with the submerged platform), they do eventually reach normal levels of performance, typically after several days [2,20]. It must be recalled that in these studies the platform location remains constant, and there are a limited number of departure points. Our results suggest that these accumbens lesioned animals had eventually learned taxis-like habits to approach the platform from each of the (typically four) departure points in the water maze.

The principal difficulty for the lesioned rats during the probe trials then was more likely related to an inability to register or recall the location of the arm with the greatest reward. There are several possible processes which could underlie this. Since the arms of the maze were identical, on probe trials when all four reward boxes were lit, there remained only room cues to guide the rat to orient to the box with the greater reward. This could have been accomplished in several different ways, as discussed by Trullier et al. [25]. In one scenario, the rats could have associated the subsequent large reward with (a) the view experienced when arriving at the choice point at the center of the maze from each of the three respective arms, and (b) the appropriate orienting movement to enter into the highly rewarded arm. Another way would be for the rat to form a map-like representation of the position of the highly rewarded box in the room, and to compare its current position and orientation with this representation to determine the appropriate orienting behavior. Of course if there were perceptible differences between the arms these too could, hypothetically, be employed as well. But such a strategy (guidance by local cues) was preserved in our accumbens lesioned rats in training trials, and the poor performance of these animals in the probe trials indicates that if this strategy was employed then, it was not done effectively.

On about 30% of the error probe trials the rats made non-random choices of orienting movements at the choice point at the center of the maze. This was observed in five of the eight lesioned rats. While the movements were inappropriate, this nonetheless shows that in these sessions, these rats were capable of programming specific orienting movements. This may be interpreted as a simple motor response strategy, which has also been shown to be preserved after hippocampal system lesions in numerous studies. All but two of the sham lesioned rats also made particular orienting movements on error trials. Thus this strategy is not completely suppressed in animals showing normal performance levels. Even in the presence of intact hippocampal-accumbal pathways there appears to be a dynamic competition among the pathways involved in the choice of goals for orientation and displacement behaviors.

Taking into account the relatively small size of the lesions, and the sparing of large parts of the Nacc shell, the performance impairments are remarkably consistent and severe. The efficacy of these small lesions may also be explained by neuroanatomical findings. The tract-tracing study of Groenewegen et al. [8] showed that afferent fibers from the hippocampus as well as magno-

cellular basal amygdala enter the accumbens dorsally through the medial shell region at locations corresponding to where our lesions were placed. Thus the behavioral changes brought on by these electrolytic lesions could well be due to destruction in these afferent pathways, as well as of the cell bodies in these regions. While in some cases the lesions also spread to other nuclei, impairment in probe trials and spared capacities in the light-guided trials were always present if there was Nacc shell damage. Even unilateral lesions had profound effects on behavioral performance (rats 2–2 and 2–3). Unilateral lesions of the dorsal striatum have also been shown to be effective in disrupting behavior [4].

The evoked potential technique proved quite useful in locating a small, elusive brain structure. A useful pilot experiment is to map in a grid of electrode penetrations the evoked potentials corresponding to respective brain structures in the region of interest. These profiles can then be used to determine and correct the lesion electrode position in trained experimental animals.

The present task should prove to be valuable for future studies in rats, and possibly in mice. It requires the animal each day to learn a new reward-place association and permits continuous dissociation of cue-guided and memory guided goal seeking. Error analyses permit the assessment of place preference and of motor habit strategies. The animals learn the task easily. Once installed, the maze is easy to operate under automatic control. Data analyses can also be carried out automatically by appropriate software analysing the timing of the rat blocking the various photodetectors. Future studies might also benefit from analyses comparing the latencies of running from the center to high and low reward arms to determine the time course of learning.

Overall our results show that the ability to acquire new knowledge about the spatial distribution of rewards requires an intact accumbens system. While rats with Nacc shell lesions are capable of retrieving rewards indicated by a visual cue, and thus they retain motivation and sensorimotor capacities. However they are impaired in locating a larger reward when the local cues are ambiguous. The choices made on error trials showed the ability to distinguish among arms in the maze, and to program specific types of reorientation movements. The deficit then seems to be in linking together information concerning reward values, information about locations and the appropriate orienting movements required to reach specific locations. This is consistent with the notion that there is convergence of location information (from hippocampus) with reward information (VTA and amygdala) in the Nacc shell, which would serve as a limbic-motor interface [15].

Acknowledgements

This work was supported by GIS, Cogniscience, a Human Frontier Scientific Program individual fellowship grant to A.B.M., a French MENRT grant to S.V.A. Thanks to F. Maloumian for preparing figures, S. Doutremer and N. Quenech'du for histology and A. Grantyn for advice for fabricating the lesion electrodes.

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