Research report

A comparison of the effects of anterior thalamic, mamillary body and fornix lesions on reinforced spatial alternation

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Abstract

The effects of cytotoxic lesions in either the anterior thalamic nuclei or the mamillary bodies were compared with those of fornix lesions on a test of spatial working memory. All three lesions impaired acquisition of a forced alternation task in a T-maze, but the disruptive effects of the mamillary body lesions were significantly less than those following either fornix or anterior thalamic damage. When the alternation task was changed, so as to increase proactive interference, the impairment associated with mamillary body damage became more evident and was now equal in severity to that in the animals with anterior thalamic lesions. The fornix lesion group were the most impaired. In contrast, all three groups performed normally on a test of object recognition. The results add weight to the view that hippocampal — anterior thalamic connections are critical for normal spatial memory and that the relative contribution of the mamillary bodies is task dependent.

Key words: Mamillary body; Anterior thalamus; Fornix; Spatial memory; Amnesia; Hippocampus; Rat

1. Introduction

Although much is now understood about the involvement of the rodent hippocampus in spatial memory, relatively little is known about the various cortical and subcortical connections that contribute to this function. As part of a series of investigations into this issue the present study compared the functions of two brain regions, the mamillary bodies and the anterior thalamic nuclei. These regions were selected because both receive substantial efferent projections from the hippocampal formation via the fornix and because lesions of the fornix mimic many of the deficits seen after hippocampal damage [2,18,19,20]. In addition, the anterior thalamic nuclei receive dense inputs from the mamillary bodies, although this projection is not reciprocated. As a consequence many of the efferent influences of the mamillary bodies depend on the anterior thalamic nuclei. This leads to the prediction that while both regions may be involved in spatial memory, the contribution of the anterior thalamic nuclei is likely to be the greater [6].

A number of previous studies have shown that lesions in the mamillary bodies or the anterior thalamic nuclei can disrupt tests of spatial memory known to be sensitive to hippocampal damage. These tests have included T-maze alternation [1,8,9,15,16,22], the radial-arm maze [23,27], the Morris water maze [26] and delayed matching and non-matching-to-position in an operant chamber [3,12]. Unfortunately, the majority of these studies have looked at either the mamillary bodies or the anterior thalamus and not directly compared the two sites. Of the few studies that have, two found evidence that anterior thalamic lesions were more disruptive than mamillary body lesions [3,26]. In these studies it was also possible to show that the spatial deficits associated with anterior thalamic lesions closely resembled those seen after fornix lesions [3,26].

A quite different pattern of results was reported, however, in a third study [16]. In this study T-maze alternation was used to compare directly the behavioural effects of mamillary body and anterior thalamic lesions [16]. It was found that anterior thalamic lesions had no effect on performance, while a significant deficit was associated with mamillary body damage [16]. Additional support for this result came from a report that cytotoxic lesions in the anterior thalamic nuclei of the mouse also had no apparent effect on spontaneous alternation in a T-maze. In contrast, other studies have found that anterior thalamic damage does correlate with a severe alternation deficit [17].
Furthermore, in the study which compared mamillary body with anterior thalamic damage the thalamic lesions were placed in either the anterior ventral or the anterior medial nuclei, but not both [16]. As a consequence the impact of the anterior thalamic lesions may have been markedly reduced. Thus it remains unclear whether spatial alternation contradicts the prediction that anterior thalamic damage will be at least, if not more, disruptive than mamillary body damage.

This issue was examined in the present study in which rats with cytotoxic lesions in either the mamillary bodies or the anterior thalamic nuclei were tested on reinforced T-maze alternation. A third group of rats with lesions of the fornix was also included. The goals of the present study were therefore: (a) to determine whether anterior thalamic lesions impair T-maze alternation; (b) to find out if the disruption differs from that observed after mamillary body damage; and (c) to compare any resultant deficits with those associated with fornix lesions.

In addition to the alternation task, which taxes spatial working memory, the animals were also given a test of object recognition [14]. In this test the animals are allowed to explore two objects, one familiar the other novel. It has been shown that normal rats will spontaneously spend more time exploring novel objects and so this can be used as a measure of the ability to recognise the unfamiliar stimulus and, hence, as a measure of non-spatial working memory [14]. The rats were tested with delays of 1 min and 15 min as both had been shown to produce reliable discrimination behaviour in normal rats [14].

2. Materials and methods

2.1. Subjects

The study involved a single cohort of 34 naive, male rats of the pigmented DA strain (Bantin and Kingman, Hull). Throughout the period of the experiment the animals were housed individually under diurnal conditions (14 h light/10 h dark), all testing occurring at a regular time during the light period. The animals were tested for 5 days a week and prior to test days fed approximately 15 g of RM1E laboratory diet (Special Diet Services, Witham, Essex). The animals' weights were monitored so that they did not drop below 85% of normal body weight. At the start of the study the animals were aged 4 months and weighed between 214-258 g. All animals had free access to water.

2.2. Apparatus

2.2.1. Experiment 1

For the forced-alternation task the animals were tested in a T-maze. The floors of the T-maze were 10 cm wide and made of aluminium. The stem was 80 cm long with a guillotine door located 33 cm from the beginning. The cross piece was 136 cm long and at each end there was a food well 4 cm in diameter and 0.75 cm deep. The walls of the maze were 17 cm high and made of clear Perspex. The maze was supported on two stands 93 cm high. Lighting was provided by fluorescent lights suspended 92 cm above the apparatus, the luminaire light levels at the choice point and food wells being 320 and 280 lx., respectively.

2.2.2. Experiment 2

The spontaneous discrimination task was carried out in a different room from Experiment 1. The apparatus consisted of a square arena (100 x 100 cm) with walls 50 cm high. The apparatus was made of aluminium and the inside surfaces were painted matt grey. The floor was covered in woodchip bedding. The objects to be discriminated, which were in triplicate, were made of glass, plastic or metal. The weight of these objects ensured that they could not be moved by the rats.

2.3. Procedures

2.3.1. Experiment 1 — spatial forced-alternation

Testing began at least two weeks after surgery by which time the animals had regained their pre-operative weight. Each animal was given several days of pretraining in order to train them to run reliably down the stem of the maze and to find food pellets in the food wells in both arms. Following this the acquisition phase began.

At the start of each acquisition trial, which consisted of two stages, three food pellets (45 mg Campden Instruments, Loughborough), were placed in each food well and a wooden block was placed at the neck of the T-maze so closing off one arm. As a consequence on each 'sample run' the animal was forced to enter the open arm where it was allowed to eat the food at the end of the arm. The animal was then picked up and confined in the start box for a delay of 10 s, during which the wooden block was removed. The door to the start box was then opened and the animal allowed a free choice between the two arms of the T-maze. On this 'choice run' the animal was deemed to have chosen when it had placed a back foot in one of the two arms, and no retracing was permitted. If the rat had alternated, i.e., had entered the arm not previously visited on the 'sample run', it was allowed to eat the food reward before being returned to its cage. If the other arm was chosen, i.e., the same arm as visited on the 'sample run', the rat was confined to that arm for approximately 10 s and then returned to its cage. The rats were tested in groups of 4 with each rat having one trial in turn, so that the intertrial interval (ITI) was about 4 min. The animals received six trials a day, for a total of twenty sessions.

The acquisition phase was immediately followed by eight
sessions on a test of continuous alternation. At the start of each of these sessions the rat was forced to either the right or the left arm and this initial sample run was rewarded with three pellets. This sample run was immediately followed by ten consecutive, massed trials in which the correct choice was always the opposite arm to the one chosen on the previous trial. The ITI was 15 s. There were no correction trials.

This was followed by a final four continuous alternation sessions, each of 12 trials. In these sessions the trials were divided equally between those with retention delays (i.e., the time spent in the start box prior to the ‘choice run’) of either 10 s, 20 s or 40 s. In this way the animals received 16 trials at each delay.

2.3.2. Experiment 2 — spontaneous discrimination of novel objects

This test began 3 weeks after completion of Experiment 1. Rats were initially given five habituation sessions in which they were allowed 3 min to explore the apparatus which was empty apart from woodchip bedding. Two days after the last habituation session the animals were tested for their exploration of familiar and novel three-dimensional objects. The rats' behaviour was monitored with the use of a videorecorder.

Each session was divided into a sample phase and a test phase. In the sample phase the rat was exposed for 3 min in the arena to a novel object and its duplicate which were placed in either far corner of the box. The rat was then removed and placed back in its own cage. After an interval of either 1 min or 15 min the rat was returned to the test arena for a further 3 min. Now there were two different objects in the far corners of the apparatus. One was identical to those used in the sample phase (i.e., it was ‘familiar’), the other was novel. An experimenter, who did not know which animal was in which group, then assessed the total time spent exploring the two objects (exploration being operationally defined as directly attending to the object with the head no more than 2 cm from the object). This procedure was used once for each of the two delays, which were tested 7 days apart. New objects were used on every occasion and the choice of sample object was varied.

2.3.3. Surgical and histological procedures

The rats were randomly allocated into four groups; anterior thalamic lesions (ATh, n = 8), mamillary body lesions (MB, n = 8), fornix lesions (FNx, n = 6) and surgical controls (SHAM, n = 12).

Animals were anaesthetized by an intraperitoneal injection (60 mg/kg) of pentobarbitone sodium. Each animal was then placed in a stereotaxic headholder (David Kopf Instruments, Tujunga) and the scalp retracted to expose the skull. A craniotomy was then made above the sagittal sinus and the dura cut above the target region.

For the anterior thalamic nuclei (ATh) lesions, injections of 0.2 µl of 0.12 M N-methyl-D-aspartic acid (NMDA) (Sigma Chemical, Poole) dissolved in phosphate buffer (pH 7.2) were made through a 1 µl Hamilton syringe into two sites in each hemisphere. The stereotaxic coordinates relative to ear-bar zero, with the incisor-bar set at + 5.0 relative to the horizontal plane, were: AP + 5.2, LAT 1.0 and AP + 5.2, LAT 1.7. The depth of the medial site was 6.2 mm below the top of the cortex, while that of the lateral site was 5.6 mm below the top of the cortex. Each injection was made gradually over a 4-min period and the needle was left in situ for a further 4 min before being withdrawn. After completion of the injections the skin was sutured and sulphanilamide powder applied.

The procedure for the mamillary body (MB) surgeries was essentially the same. The only difference was that the animals received only one injection of 0.5 µl of 0.12 M NMDA per hemisphere. The coordinates of these injections relative to ear-bar zero, with the incisor bar set at + 5.0, were AP + 3.2 and LAT 0.7. The height was 9.8 mm below the cortex.

The initial stages of the fornix lesions (FNx) were the same as those for the ATh and MB surgeries, but the actual lesion was made by radiofrequency. A Radionics TCZ (Radionics, Burlington) electrode (0.3 mm tip length and 0.25 mm diameter) was lowered vertically into the fornix and the tip temperature raised to 75 °C for 60 s using an RFG4-A Lesion Maker (Radionics, Burlington). Two lesions were made in each hemisphere. The stereotaxic coordinates of the lesions relative to ear-bar zero, with the incisor bar set at + 5.0, were AP + 5.3, HT + 7.1, LAT 0.7 and AP + 5.3, HT 7.0, LAT 1.7.

Those animals (SHAM) who were surgical controls for the ATh, MB, and FNx groups received a craniotomy over the midline sinus. The position of this overlapped with that used for all three lesion groups. The dura was then cut as in the lesion surgeries. Following this the skin was sutured and each animal received sulphanilamide powder.

On completion of the experiment the animals were killed and perfused intracardially with 0.9% saline followed by 5% formol-saline. The brains were then rapidly removed and placed in 5% formol-saline. Subsequently, the brains were blocked, embedded in wax (Paraplast) and cut into 10 μm coronal sections. Every tenth section was mounted and stained with cresyl violet, a Nissl stain.

3. Results

3.1. Histological analysis

All of the anterior thalamic lesions (ATh) produced extensive bilateral damage in the anterior medial, anterior
ventral and anterior dorsal nuclei (Figs. 1 and 2). In one animal there was a vascular accident which extensively damaged the cortex in one hemisphere and this animal was excluded from the study. The anterior thalamic damage in the remaining seven animals was most marked in the anterior medial nucleus which appeared to have been completely damaged in all but two cases. Cellular sparing in the anterior ventral nucleus was typically confined to the

Fig. 1. Diagrammatic reconstructions showing the extent of the anterior thalamic (ATH), mamillary body (MB) and fornix (FNS) lesions. Areas in black show complete loss of neurons, while stipled areas show regions of partial cell loss. The top two rows depict the smallest (upper) and largest (lower) of the ATh lesions, the next two rows show the smallest (upper) and the largest (lower) of the MB lesions. The bottom row shows the extent of the largest (diagonal lines) and smallest (black) FNS lesions. The sections are modified from Pellegrino and Cushman [21] and the numbers correspond to the approximate position from Bregma. Abbreviations: F, fornix; RE, nucleus reuniens; SUM, supramamillary nucleus.
Fig. 2. Photomicrographs of coronal sections (Nissl stain) through the right anterior thalamus in an ATh (upper) and a SHAM (lower) case. The ATh case shows a typical amount of shrinkage and neuronal loss in the anterior thalamic nuclei. The arrow points to a small region of sparing in the anterior ventral nucleus. Abbreviations: AD, anterior dorsal nucleus; AM, anterior medial nucleus; AV, anterior ventral nucleus; F, fornix; V, ventricle. Both sections were photographed at the same magnification but the injections in the ATh case led to marked shrinkage of much of the dorsal thalamus.
more lateral part of the nucleus (Fig. 2). There was more variable damage in the anterior dorsal nucleus and this nucleus was completely spared in one case. The rostral part of the lateral dorsal nucleus was involved in five animals (unilaterally in three cases and bilaterally in two cases). In addition, all animals showed cell loss in the non-specific nuclei (paraventricular, reunions and parataenial) adjacent to the anterior nuclei, but in two cases this damage was very minor. Nucleus medialis dorsal is was involved in only two animals and in these cases the lesion only involved the rostral tip of the nucleus. In some cases the lesion resulted in minor disruption of fornical fibres immediately above the injection site (Fig. 2).

The mamillary body lesions (MB) proved to be highly selective, the region of cell loss being almost completely confined to the mamillary region (Fig. 1). In one case the neurotoxin only produced irregular patches of cell loss in the mamillary bodies and this animal, whose pattern of cell loss was quite different to the others, was discarded from the study. In all other seven cases there was extensive cell loss throughout the medial and lateral mamillary nuclei (Figs. 1 and 3). In five of these cases there appeared to be a loss of at least 90% of the cells in the lateral, medial and posterior mamillary nuclei. In four of these cases the cell loss was almost complete. In two animals the lesion extended dorsally to involve much of the supramamillary nucleus. The anterior thalamic nuclei appeared normal in all MB animals.

The fornix lesions (FNx) produced extensive damage to the fibre tract itself and in most cases also extended into the most rostral head of the hippocampus. In one case the tract was completely severed but in the remainder the lateral tips of the fimbria were spared (Fig. 1). In all cases the lesion damaged part of the corpus callosum and in three animals the cingulum bundle was partially interrupted. The dorsal margin of the anterior thalamic nuclei was damaged in one case.

Following histological analysis the study consisted of twelve SHAM, seven ATh, seven MB and six FNx animals.

3.2. Experiment 1: spatial forced-alternation

During the initial 20 acquisition sessions each animal performed a total of 120 trials with a retention delay of 10 s (Fig. 4). Scores were analyzed using an ANOVA in which the acquisition phase was divided into five blocks, each of four sessions. The comparison provided evidence of a highly significant group effect \(F_{3,28} = 27.4, P < 0.001\). There was, in addition, a highly significant effect of trial block \(F_{4,112} = 13.9, P < 0.001\), reflecting the improvement in performance during acquisition of the task, but there was no group x trial block interaction \(F < 1\).

Subsequent comparisons between the overall scores of the four groups using the Newman–Keuls test confirmed the expected deficit in the FNx group (FNx vs. SHAM \(P < 0.001\)). In addition, it was found that the FNx group differed from the MB animals \(P < 0.001\) but not from the ATh group. It was also found that the ATh group were significantly impaired when compared with both the SHAM \(P < 0.001\) and the MB \(P < 0.01\) groups. Finally, it was found that MB group were impaired relative to the SHAM animals \(P < 0.01\).

The animals were then tested for eight sessions (80 trials) on the continuous alternation procedure (Fig. 4). A comparison of the total number of correct score revealed a clear group effect \(F_{3,38} = 19.4, P < 0.001\). Subsequent analyses using the Newman–Keuls test indicated that the FNx group performed worse than all of the other three groups \(P < 0.01\) and that both the ATh and the MB groups differed from the SHAM animals \(P < 0.001\).

There was, however, no difference between the scores of the ATh and MB groups.

The third condition assessed the performance of the three groups on the continuous alternation task using delays of 10 s, 20 s and 40 s between trials (Fig. 4). An analysis of variance with the factors groups and delays revealed evidence of a lesion effect \(F_{3,28} = 8.32, P < 0.001\) and of an effect of delay \(F_{2,56} = 26.35, P < 0.001\). There was, however, no interaction between these two factors \(F_{5,56} = 1.09\). Comparisons between the scores of the four groups (Newman–Keuls) revealed that the FNx group \(P < 0.001\), the ATh group \(P < 0.05\) and the MB group \(P < 0.05\) all differed from the SHAM animals, but that no other comparisons were significant.

A final analysis took the combined scores from all three of the T-maze conditions. As expected there was a highly significant group effect \(F_{3,28} = 30.0, P < 0.001\). Subsequent comparisons between the four groups (Newman–Keuls) revealed that the FNx animals scored significantly lower than all three other groups, that the ATh group were worse than the MB \(P < 0.05\) and the SHAM \(P < 0.001\) groups, and that the MB group were worse than the SHAM group \(P < 0.001\).

3.3. Experiment 2: spontaneous object recognition

The initial analysis sought to determine whether there were any group differences in the overall levels of exploration, independent of the recognition performance. We therefore compared the total time spent exploring the two identical objects in the sample phase and as the situation in the sample phase was identical for the 1 min and 15 min conditions these times were combined. There was no clear evidence of a group difference \(F_{3,28} = 2.28, P = 0.082\) on the baseline levels of exploration.
Fig. 3. Photomicrographs of coronal sections (Nissl stain, same magnification) through the mamillary body region in an MB (upper) and a SHAM (lower) case. The upper section shows a typical amount of shrinkage and gliosis in the mamillary body region of an MB animal. Abbreviations: MM, medial mamillary nucleus; V, ventricle.
Following this the performance of the animals on the test phase was examined. Recognition scores were calculated by subtracting the time spent exploring the familiar object from the time spent exploring the novel object. Positive difference scores therefore correspond to a bias to the novel stimulus and hence are evidence of successful discrimination between the two stimuli (Fig. 5). These difference scores were analyzed in a two-way analysis of variance with the factors delay (1 min or 15 min) and group. This analysis indicated that there were no group effects ($F_{3,28} = 1.89$), but there was a small effect of delay ($F_{1,28} = 4.47, P < 0.05$) with the discrimination scores improving after the delay of 15 min. There was no group by delay interaction ($F_{3,28} = 1.35$).

In view of the suggestion of a difference in baseline levels of exploration ($0.05 < P < 0.1$) the discrimination scores were recalculated using a recognition ‘index’. This index was the difference in exploration time between the novel and familiar object calculated as a percentage of the total time spent exploring both objects. A subsequent analysis of variance showed once again that there was no lesion effect ($F < 1$) and no interaction ($F < 1$), but now there was also no delay effect ($F < 1$).
Analysis of the groups scores using either the difference
time or the discrimination index showed that all four
groups favoured the novel object after 1 min (95% con-
fidence limits) and that all but the ATh group discrimi-
nated after 15 min.

4. Discussion

The present study had three goals. The first was to
determine whether lesions of the anterior thalamic nuclei
disrupt T-maze alternation. This was clearly confirmed as
the ATh group were impaired, relative to the SHAM group,
on all three phases of the alternation task. The second goal
concerned comparisons with the mammillary body lesion
and that revealed two different patterns of results.
During the initial acquisition stage the ATh animals were
more impaired than the MB animals, but during the con-
tinuous alternation tests the two groups could not be dis-
tinguished. These findings support the prediction that
anterior thalamic lesions will be at least as disruptive as
mammillary body lesions on tests of spatial memory.
The third goal was to compare the diencephalic deficits with
those found after fornix damage. While the effects of an-
terior thalamic damage most closely resembled those as-
associated with fornix lesions, it was also the case that the
FNx animals were significantly more impaired on the con-
tinuous alternation tests.

The deficits in the ATh animals strongly indicated that
the anterior thalamic nuclei are necessary for the normal
performance of spatial alternation tasks [17]. The finding
that anterior thalamic damage disrupts other spatial tests
adds weight to this view [3,6,26] and supports the more
general conclusion that the anterior thalamic nuclei play
an important role in the processing of spatial information
by the hippocampus [6]. It should be added that the im-
pairment in the ATh group could not be correlated with
damage in any other thalamic region, although additional
studies may be required to test for a contribution from
the rostral midline thalamic nuclei. These nuclei are of inter-
est as they, like the anterior thalamic nuclei, have recip-
rocral connections with the hippocampus. Lastly, the
present findings emphasized the need to consider the pos-
sible involvement of the anterior thalamic nuclei when
analyzing the consequences of other thalamic lesions on
tests of spatial memory [17].

While there is both anatomical and lesion evidence indi-
indicating that the anterior thalamic nuclei are important for
spatial working memory, there are some conflicting find-
ings from lesion studies [10,11,16]. As has already been
pointed out, in one of these studies the lesions were only
targeted at one of the anterior thalamic nuclei [16] and it
is likely that this explains the lack of any clear deficit. In

a second study, in which mice received ibotenic acid lesions
of the anterior thalamic nuclei and were tested for sponta-
aneous alternation, the findings were based on just 15
trials [10]. This means that the lack of any lesion effect
must be treated with caution. It is less clear why anterior
thalamic lesions should have failed to disrupt radial-arm
maze acquisition [11], but an important variable may pro-
ve to be the extent of the anterior thalamic damage.

The performance of the MB group reinforced previous
studies showing that mammillary body lesions can impair
tests of spatial memory [23,26,27], including T-maze al-
ternation [1,8,9,15,16,28]. It was also apparent that in the
acquisition stage the MB deficit was less than that in the
ATh group. This is consistent with the notion that the
direct hippocampal afferents to the anterior thalamic nu-
clei, i.e., those that bypass the mammillary bodies, are im-
portant for normal spatial memory [6]. The significance
of these direct projections is highlighted not only by the dif-
fERENCE in the acquisition scores of the MB and ATh ani-
mals, but also by the results from an automated non-
matching-to-position task in which anterior thalamic, but
not mammillary body, lesions were associated with a clear
performance deficit [3]. Furthermore in that study, the
anterior thalamic deficit was virtually indistinguishable
from that associated with fornix lesions [3], again under-
lining the importance of these direct projections.

A particularly interesting feature of the results was that
the switch to continuous alternation led to a more marked
impairment in the MB group, so that the deficits in the MB
and ATh groups now became comparable. One explana-
tion for this finding is that the contribution from the
mammillary bodies becomes particularly important when
levels of interference are high. This would suggest that the
mammillary bodies aid the temporal separation of test trials.
This view is consistent with a number of other studies on
the interaction between the effects of mammillary body dam-
age and levels of interference [8,9]. There is also evidence
that these mammillary body effects can be attenuated by
providing distinctive contextual cues to help separate tri-
als [9,28]. This may account for the relatively good per-
formance of the MB animals on the acquisition stage as
the trials were not only spaced, the animals were also
placed in their home cages during the ITI. While such
findings are clearly suggestive of a contribution specific to
interference it is still the case that the pattern of MB
deficits could merely reflect task difficulty [27]. The find-
ing that mammillary body lesions can disrupt performance
on the Morris water maze [26], in which there is little
interference, also suggests that increased sensitivity to in-
terference may not be a sufficient explanation of the effects
of mammillary body damage.

In view of the extensive hippocampal inputs to both the
mammillary bodies and the anterior thalamic nuclei it was
of interest to compare the ATn and MB animals with the FNx rats. On all of the spatial alternation tasks the impairment associated with fornical damage was significantly greater than that found in the mamillary body group. In contrast, the ATn group did not differ from the FNx animals during the 20 acquisition sessions, although significant differences did emerge on the subsequent, continuous alternation tasks. Thus the acquisition findings, in particular, serve to emphasize the importance of the hippocampal-diencephalic connections for normal spatial memory and highlight the role of the anterior thalamic nuclei. The significant differences that were found during the continuous alternation tasks may indicate that other fornical afferents contribute to spatial memory or that septal afferents to the hippocampus add to the fornical deficit on this particular task. Another possibility is that animals with fornix damage show more perseverative behaviour than those with diencephalic lesions. This should be considered as such behaviour, e.g., persistently turning to one side, would prove particularly ineffective on the continuous alternation task and lead to scores below chance. It should also be noted that the ATn lesions spared much of the lateral dorsal nucleus, even though this nucleus is sometimes regarded as part of the anterior thalamic nuclei with which it shares many similar connections [7]. Clearly damage to this region might increase the anterior thalamic deficit, but this needs to be confirmed.

The animals were also given a non-spatial test of working memory. This indicated that the diencephalic lesions did not disrupt object recognition, although delays longer than 15 min were not assessed. The findings for the FNx and MB groups were consistent with other studies showing that these lesions need not impair delayed non-matching-to-sample performance [1,24]. Taken together, these preliminary findings suggest that the deficits associated with anterior thalamic and mamillary body lesions are most evident on spatial tasks.

A final aspect of this study concerns its relevance for research into the neural systems responsible for anterograde amnesia [6]. In particular, the results strengthen the notion that the hippocampus forms a functional system with the mamillary bodies and the anterior thalamic nuclei and that this system is important for certain aspects of memory. This in turn suggests that previous reports may have underestimated the significance of the direct hippocampal — thalamic system to anterograde amnesia [25,29]. The results also indicate that if damage to the mamillary bodies contributes to anterograde amnesia [13] then the effects of anterior thalamic injury should prove at least, if not more, severe [6]. While studies of lesions in monkeys support this view [4,5], confirmation of this prediction will have to await the testing of appropriate clinical cases.

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References


