will thus be very small, therefore the stimulation of the lateral line by the mechanism discussed here will be of litle consequence. This means that lateral line systems should be disturbed little by most of the background noises in the sea[4,6,12].

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Place navigation impaired in rats with hippocampal lesions

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Electrophysiological studies have shown that single cells in the hippocampus respond during spatial learning and exploration[1–4], some firing only when animals enter specific and restricted areas of a familiar environment. Deficits in spatial learning and memory are found after lesions of the hippocampus and its extrinsic fibre connections[5,6] following damage to the medial septal nucleus which successfully disrupts the hippocampal theta rhythm[7], and in senescent rats which also show a correlated reduction in synaptic enhancement on the perforant path input to the hippocampus[8]. We now report, using a novel behavioural procedure requiring search for a hidden goal, that, in addition to a spatial discrimination impairment, total hippocampal lesions also cause a profound and lasting place-navigational impairment that can be dissociated from correlated motor, motivational and reinforcement aspects of the procedure.

If rats are placed in a large circular pool of opaque water, they will quickly learn to escape by finding and climbing on to a small platform hidden beneath the water surface, provided it remains in a fixed location over a series of trials[9]. They cannot learn to find it when its position varies randomly from trial to trial. Although they can never see, hear or smell the platform, rats require only a few trials in order to learn to swim directly towards it, using the shortest route, even from a novel starting place. That is, the rats learn not only to recognize the vicinity of the safe place when they reach it, but also to swim towards it from a distance despite the absence of cues from the platform itself. The deleterious effects of cue–response separation apparent in visual discrimination[10,11] do not, in this case, prevent extremely rapid learning. By comparing the performance of normal and brain-lesioned animals in these conditions with that shown when a fixed but visible platform was used, we have examined the role of the hippocampus in simple navigation.

Female Lister rats ($n = 31$) were subjected to the following procedures: total hippocampal lesions ($n = 10$), superficial cortical lesions ($n = 13$), sham surgery ($n = 4$) or no surgery ($n = 4$). The rats were placed, under pentobarbitone anaesthesia, into a special adjustable head-holder[12]. Animals in the hippocampal lesion group had holes drilled in their skulls, and a small amount of neocortex overlying the hippocampus, and the entire dorsal and ventral hippocampus were removed by aspiration. Operated control animals had comparable lesions in the neocortex but showed no hippocampal damage. Sham-operated control animals had burr holes drilled in their skulls but suffered no brain damage. On completion of the behavioural procedures, conventional histological techniques (40 μm, gelatine-embedded sections stained with cresyl violet and solochrome cyanide) were used to verify the lesions. All rats of the hippocampal-lesion group were found to have total or near total destruction of the dorsal and ventral hippocampus, with minimal damage to adjacent structures (comparable lesions are reported in ref. 13). Analysis of the behavioural data showed no differences between the sham-operated and unoperated control groups, which were therefore combined, giving final group sizes of 10 (hippocampal), 13 (cortical) and 8 (control).

On day 1, the rats were placed in a pool of water (1.32 m diameter, 53 l at 26 ± 1 °C) and allowed to swim freely for 1 min with no opportunity for escape. On day 2, a platform was hidden in one of four locations in the middle of each cardinal quadrant (SW, NW, NE and SE), 0.33 m from the side walls. Different locations were used for different rats. The platform, made of clear perspex, was hidden by adding 2.3 l of milk to the water and arranging for its top surface, 8 cm in diameter, to be 1 cm below the water level. A second platform, 2 cm taller and protruding visibly out of the water, was used at a later stage of training; its top surface was indented such that it contained within its circumference a 1 cm layer of water. Thus, the reinforcement afforded by escape on to the two platforms was equated. The rat's task throughout the training procedures, which continued for 8 days, was to find and escape on to the platforms. Only one platform was used at a given stage of training, and it was always in a fixed position in the pool on a given day. Thus the two tasks, which we shall call place-navigation and cue-navigation, respectively, involved the same motor movements (swimming), motivation and reinforcement (escape from water), but differed specifically and uniquely with respect to whether or not the rat was required to learn the platform's position in relation to the varied distal room cues.

All rats swam effectively using the characteristic adult swimming posture[14]. The times taken to escape from the water during the three successive phases of the experiment are shown in Fig. 1. The normal and cortical-lesion groups learned to escape rapidly from the water with stable terminal acquisition latencies of < 8 s. The hippocampal-lesion group showed a highly significant impairment in the place-navigation task (trials 1–28) when the hidden platform was used. However, this impairment declined dramatically and disappeared when the visible platform was used (trials 30–41), this platform having been placed diagonally opposite to the earlier training location (that is, NW for a rat trained previously to find the hidden platform at SE). The place-navigation impairment reappeared when training was continued with the hidden platform (trials 43–50) even though it remained in the same position that the visible platform had occupied in the preceding phase of training.

Detailed analysis of the behavioural performance of each group and the results of two transfer tests provide new insights into the nature and magnitude of the deficit after hippocampal lesions. First, the hippocampal-lesion animals did improve during training but never escaped faster than normal animals searching for a hidden platform that was moved around randomly from place to place on successive trials (see Fig. 1, horizontal broken line, taken from ref. 9). Second, analysis of the paths taken by all rats on trial 28, transcribed from videotape recordings, showed that the hippocampal-lesion animals took longer and more circuitous routes to find the hidden platform

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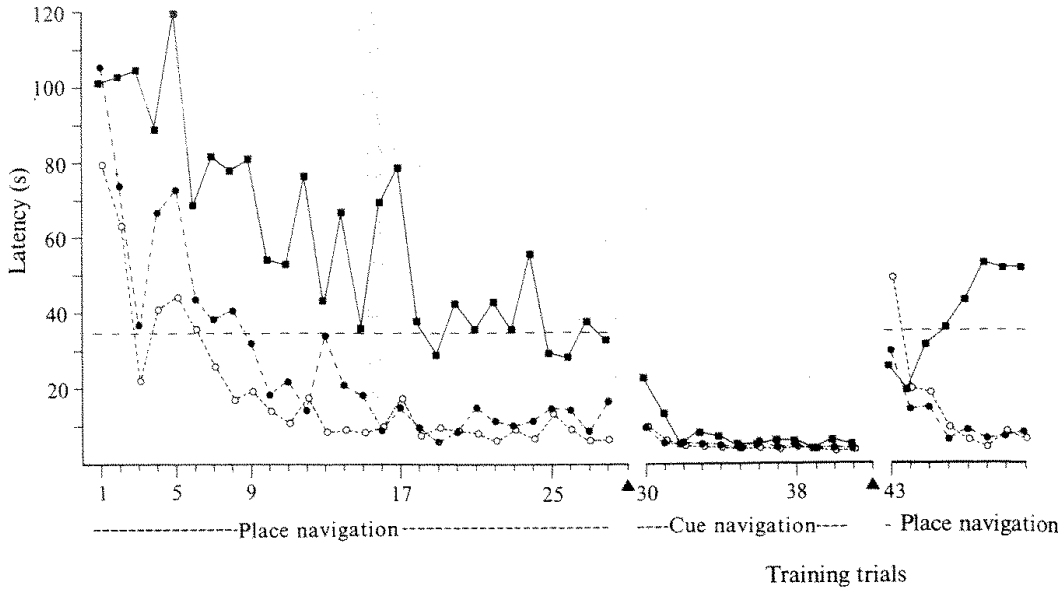

Fig. 1 Mean latency of escape (s) for the 50 trials of the experiment. ■, Hippocampal lesion; ●, cortical lesion; ○, control;. The trial number of the first of each daily set of trials is shown on the abscissa. The two transfer tests are indicated by solid triangles. To avoid problems of heterogeneity of variance, the successive phases of the experiment were analysed separately. The horizontal broken line (trials 1–28 and 43–50) at 34.5 s corresponds to the best performance shown by a group of normal rats trained to search in 20 trials for a hidden platform that was moved randomly from one place to another over successive trials (data taken from ref. 9). Place navigation (trials 1–28): unweighted means (unequal n) analysis of variance revealed significant effects of group ($F = 23.7$, d.f. = 2/28; $P < 0.0001$), trials ($F = 17.8$, d.f. = 23/667; $P < 0.0001$) and lesion × trials ($F = 1.5$, d.f. = 54/756; $P < 0.02$). Subsequent orthogonal comparisons showed that the deficit was restricted to the hippocampal-lesion rats (hippocampal versus cortical + control, $P < 0.0001$; cortical versus control, $P > 0.10$). Cue navigation (trials 30–41): terminal escape latencies (trial 41) were 5.0, 3.3 and 2.8 s for the hippocampal-lesion, cortical-lesion and control groups respectively, corresponding to declines relative to trial 28 of 45.9, 7.9 and 3.7 s). Analysis of variance of all 12 trials revealed a small residual impairment in the hippocampal-lesion groups ($F = 5.4$, d.f. = 2/28; $P < 0.02$). Return to place navigation (trials 43–50): analysis of variance showed a highly significant effect of groups ($F = 12.2$, d.f. = 2/28; $P < 0.0002$) and a lesion × trials interaction ($F = 3.6$, d.f. = 14/196; $P < 0.0001$). The apparent gradual impairment of performance in the hippocampal-lesion group was caused by a slowing of swimming speed over trials as the core temperature of the rats fell slightly (from 37 °C to ~35 °C).

(Fig. 2). The directional heading of the hippocampal-lesion rats when they set off from their starting position on trial 28 was no more likely to be towards the platform than in any other possible direction. These results imply that hippocampal-lesion rats can learn some sort of escape strategy (for example, that escape is possible) but are substantially poorer at learning where the hidden platform is located and, unlike normal and cortical-lesion animals, will never learn to swim towards it from a distance.

The magnitude of this place-navigational deficit was assessed in two separate transfer tests conducted on trials 29 and 42, immediately after the four daily trials of days 6 and 8. For transfer test A, the hidden platform was first removed from the apparatus, then the rats were placed in the pool for 60 s with no opportunity for escape, and their movements observed. The results were striking. Control and cortical-lesion rats swam to and persistently across the former platform location whereas the hippocampal-lesion rats did not. The hippocampal-lesion rats did not merely swim around the side walls. To demonstrate this, annuli were marked on the video screen indicating the exact surface area and former positions of the platforms in each of the four cardinal quadrants. The total number of annuli which an individual rat passed through during the 60-s test was 7.6, 6.8 and 8.6 for the hippocampal-lesion, cortical-lesion and control groups, respectively ($F < 1$). The groups were distinguished by which annuli they passed through: an individual hippocampal-lesion rat was no more likely to pass through the annulus marking the platform position used during training than one in any other quadrant (Fig. 3*a*). We observed no tendency on the part of the hippocampal-lesion rats to remain in the vicinity of the training annulus once they had eventually reached it (compare with ref. 7). Thus the deficit produced by hippocampal lesions was total. Furthermore, with respect to the lack of spatial bias revealed in the annulus measure, the deficit was apparent in all 10 rats of the experimental group.

Our interpretation of these findings is that, whatever their other effects[15–19], hippocampal lesions do cause a profound and lasting place-navigational impairment. It could be argued, however, that while matched for motor requirements, motivation and reinforcement, the place- and cue-navigational tasks are not matched for task complexity. Perhaps hippocampal-lesion animals perform poorly on the spatial task because it is complex (albeit a task learned by normal animals in less than 10 trials), and perform better on the visible platform task because it is easier, rather than because the spatial component is then redundant. If this is the basis of the dissociation of effects in the two tasks, then at least some spatial bias should be shown by some of the hippocampal-lesion animals in a transfer test conducted after training on the ostensibly easier visible platform task. Transfer test B, conducted immediately after trial 41 on day 8, examined this possibility. In trial 41 itself, there was no significant difference in the latency, path-length or directionality of escape behaviour across groups ($F_s < 1$), all animals escaping rapidly by means of short, direct paths to

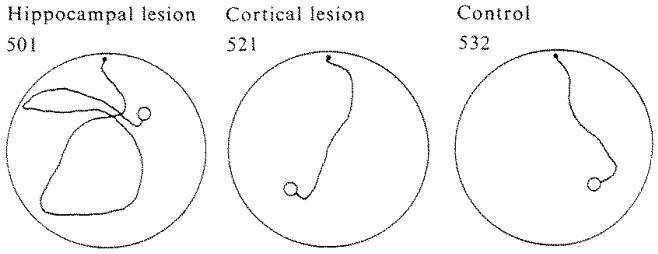

Fig. 2 The actual path of the median rat (defined in terms of path length) in each group on trial 28 just before the first transfer test. The rats were observed using a video camera placed above the pool. One experimenter (P.G.) sat concealed in one corner of the room and monitored the rat's movement on a VTR recorder. The second experimenter (R.M.) removed each rat from its home cage in an adjacent room and placed it in the pool. The pool was open to the room which included a door, a window, and brightly and darkly lit walls. The paths taken by the rats in escaping were transcribed from the videotape and measured. Path lengths: the hippocampal-lesion rats took 4.66 ± 0.86 m to reach the platform, whereas the cortical-lesion and control rats took 2.35 ± 0.98 and 1.20 ± 0.34 m, respectively. Analysis of variance showed that these path lengths differed significantly ($F = 4.23$, d.f. = 2/28; $P < 0.025$). Subsequent orthogonal comparisons showed that the hippocampal-lesion group took significantly longer paths than both the cortical-lesion and control groups ($P < 0.001$), which in turn did not differ significantly from each other ($P > 0.10$). Directionality: the accuracy of the approach to the platform was analysed as follows. We measured the angle subtending a tangent to the rat's path at a point 0.5 m from its starting position, and a line intersecting this point and the centre of the platform. This angle was 83 ± 18° from the correct direction for the hippocampal-lesion group, whereas for the cortical-lesion and control groups, the angle was 34 ± 13° and 38 ± 17°, respectively (Kruskal–Wallis, $H = 5.87$, d.f. = 2; $P < 0.025$, one-tailed).

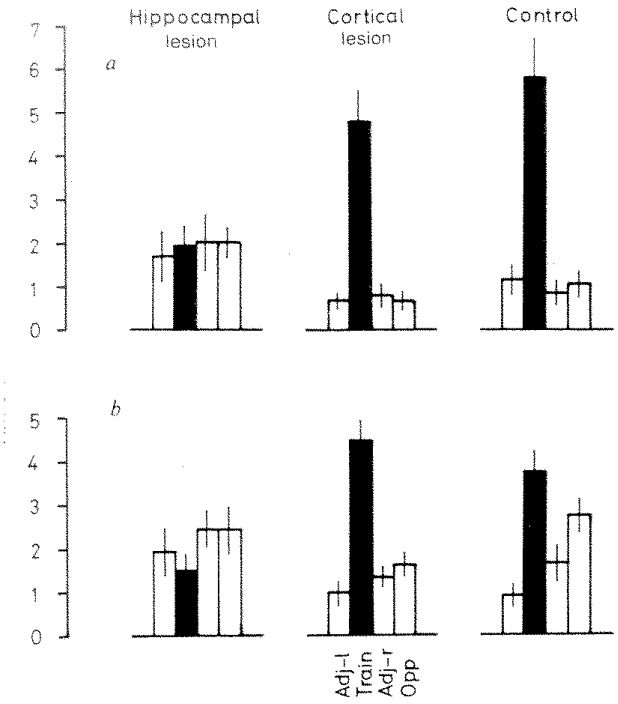

Fig. 3 Mean crossings of each of the annuli (± 1 s.e.) marking the former platform positions during *a*, transfer test A (after place-navigation training) and *b* transfer test B (after cue-navigation training). The data have been categorized for each animal into crossings of the training location (Train), and of the annulus in the adjacent quadrant to the left (Adj-l; viewed from above), the adjacent right (Adj-r), and opposite quadrant (Opp). Note that the hippocampal-lesion rats were no more likely to pass through the annulus marking the training position than any other, in both transfer tests. Analyses of variance showed a highly significant groups x position effect in both transfer test A ($F = 10.1$, d.f. = 6/84; $P < 0.0001$) and transfer test B ($F = 9.5$, d.f. = 6/84; $P < 0.0001$).

he visible platform. However, in the transfer test conducted 0 s later, only the control and cortical lesion groups searched n the vicinity of the now absent but previously visible platform Fig. 3*b*). All 10 animals in the hippocampal-lesion group howed no spatial bias. Thus even if the improvement by the ippocampal-lesion group in the visible platform phase of train-ng was due to the simplicity of the task, this improvement was ot accompanied by any spatial learning.

The procedures used here provide a new approach to analys-ng the brain mechanisms of spatial localization. The results how that hippocampal lesions cause a profound and lasting mpairment in place-navigation and question that aspect of the vorking-memory hypothesis[17] which asserts that spatial refer-nce memory is unaffected by septo-hippocampal damage. Reference memory has been defined as those aspects of a earning procedure in which learned information may be used n every trial of training rather than for just a single trial. The resent procedure using a fixed platform position for 28 trials, ollowed by different fixed position for 20 further trials, is ertainly a reference-memory procedure. In the absence of eparate measures of working memory in this experiment, we annot comment further on the adequacy of that hypothesis. However, we suspect that claims about the integrity of spatial eference memory after more restricted fimbria-fornix lesions nd extensive preoperative training[20] may provide a misleading icture of normal hippocampal function.

The present results show that normal rats can navigate in an ppropriate direction towards a hidden object; they do not nerely recognize a place when they reach it. Whether this type of learning involves or is different from conventional associative earning deserves further scrutiny. But given that place units detected so far in the hippocampus[1-4] respond only with respect to places in which the rat is presently situated as opposed to places to which it intends to go, these results pose a challenge for electrophysiologists attempting to explain the neural mechanisms by which the hippocampus processes spatial information.

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Evidence for dendritic competition in the developing retina

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At present little is known of the rules regulating dendritic morphology. Several studies have demonstrated that the shape of the dendritic tree depends on its afferent supply[1,2]. The ganglion cells of the retina provide a particularly useful cell type for the study of neurone development as they develop independently of afferents from other brain regions. If the ganglion cells alone are destroyed in a small patch of the developing retina, it is possible to examine how the absence of neighbouring neurones of the same type influences the development of the ganglion cells around the depleted area. The development of the normal laminar pattern of the retina is not disturbed by the loss of these cells[3]. We show here that the dendrites of ganglion cells around the depleted area are preferentially directed towards this region. The orientation of ganglion cell dendrites is strongly influenced by neighbouring cells and we suggest that during normal development, dendrites compete for their afferents.

Experiments were performed on 11 hooded Lister rats. On the day of birth, the rats were anaesthetized by hypothermia and a small lesion was made in the temporal retina of one eye using a fine 28-gauge needle passed through the sclera approximately half-way between the optic disk and the limbus. After 2–3 months, the animal were anaesthetized with an intraperitoneal injection of 3.0 ml per kg of chlor-nembutal (2.1 g of chloral hydrate + 0.5 g of sodium pentobarbital in 50 ml of 0.9% saline). A series of six injections of 0.15–0.25 μl of horseradish peroxidase (HRP; Boehringer) (50% w/v in 2% dimethyl sulphoxide) were made stereotaxically into the optic tract, using a 1-μl Hamilton syringe. The animals were killed painlessly after 24 h, perfused with 0.9% saline and the eyes removed. The retinae were prepared as whole mounts[4], and reacted in a modified Hanker–Yates solution[5]. After washing in 0.1 M phosphate buffer (*p*H 7.2) for several hours, each retina was transferred to 50 ml solution of 0.1 M sodium

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