been interpreted by Y. Fugita [*Brain Res.* **175**, 59 (1979)] as a remote IPSP. Our results indicate that this potential is neither primarily chloride-dependent nor mediated by GABA, although it may be remote. R. H. Thalmann and G. F. Ayala [*Neurosci. Abstr.* **6**, 300 (1980)] arrived at the same conclusion regarding the late hyperpolarization after orthodromic stimulation in CA1 cells and observed similar potentials in CA3 pyramidal cells and in granule cells of the dentate gyrus. We would agree with Fugita that the response is in the olfactory cortex, a late hyperpolarization with many features similar to the one we report has been described [K. Mori, M. Satoh, S. F. Takagi, *Proc. Jpn. Acad. Ser. B.* **54**, 484 (1978); A. Constanti, J. D. Connor, M. Galvin, A. Nistri, *Brain Res.* **195**, 403 (1980)].
13. C. Cotman, in *Glutamate as a Neurotransmitter*, G. DiChiara and G. L. Gessa, Eds. (Raven, New York, 1980).
14. The hyperpolarization following the glutamate depolarization usually had a reversal potential approximately 5 to 10 mV more positive than the afterhyperpolarization following direct depolarizing current pulses. This difference is probably due to a residual glutamate depolarization during the early part of the hyperpolarizing response.
15. We have not determined if the reduction in the hyperpolarization is due to lack of calcium or to the presence of calcium antagonists. Calcium antagonists are known to pass through excitatory transmitter channels at peripheral synapses and thus, if the antagonists are exerting an effect, it may be occurring at an intracellular site (*2*).
16. P. Ascher, A. Marty, and T. O. Neild [*J. Physiol. (London)* **278**, 177 (1978)] noted that acetylcholine activates a calcium-dependent potassium current in *Aplysia* neurons. Glutamate-induced afterhyperpolarizations associated with a conductance increase have also been reported in dissociated spinal neuron cultures (J. M. Wojtowicz, M. Gysen, J. F. MacDonald, *Brain Res.*, in press) and in cells of the olfactory cortical slice [A. Constanti, J. D. Connor, M. Galvin, A. Nistri, *ibid.* **195**, 403 (1980)].
17. P. A. Schwartzkroin and M. Slawsky, *Brain Res.* **135**, 157 (1977); R. K. S. Wong, D. A. Prince, A. I. Basbaum, *Proc. Natl. Acad. Sci. U.S.A.* **76**, 986 (1979).
18. J. P. Gallagher, H. Higashi, S. Nishi, *J. Physiol. (London)* **275**, 263 (1978). The precise electrotonic structure of these cells is not fully understood, but it appears there is a general consensus that the apical dendrites of these cells, which extend 500 to 600 μm from the cell body, are less than one space constant in electrotonic length [see, for example, D. A. Turner and P. A. Schwartzkroin, *J. Neurophysiol.* **44**, 184 (1980)]. We studied glutamate responses produced within 100 μm of the cell body and which, therefore, are quite close to the clamp electrode.
19. The coupling of the hyperpolarization with the preceding depolarization suggests that the hyperpolarization occurs as a consequence of the depolarization. It might be proposed that the glutamate depolarization of the pyramidal cell activates a reciprocal synaptic inhibition [C. E. Jahr and R. A. Nicoll, *Science* **207**, 1473 (1980)] mediated by a transmitter that feeds back onto the pyramidal cell and increases potassium conductance. However, the fact that voltage clamping the glutamate depolarization does not reduce the response indicates that such a pathway cannot account for the hyperpolarization.
20. L. G. Brock, J. S. Coombs, J. C. Eccles *J. Physiol. (London)* **117**, 431 (1952) (see figure 8).
21. J. S. Coombs, J. C. Eccles, P. Fatt, *ibid.* **130**, 374 (1955) (see figures 8 and 9).
22. Supported by grant NS 15764, RCDA NS-00287 to R.A.N. and NIH training grant NS07067 to B.E.A.

10 October 1980; revised 15 December 1980

Rapid Forgetting of a Spatial Habit in Rats with Hippocampal Lesions

Abstract. *Rats with lesions of the hippocampus or mammillary bodies were impaired in learning reversal problems in a T-maze. Test trials given after learning each reversal disclosed little forgetting in the mammillary body group but rapid forgetting in the hippocampal group. These findings resemble those recently reported in patients with amnestic syndromes.*

It has been known for a number of years that humans suffering damage to either the medial temporal region (including the hippocampus) or the diencephalon (particularly the mammillary bodies, medial thalamus, or both) exhibit a dramatic disturbance in memory, commonly called the "amnestic syndrome" (*1*). Patients with these lesions may show virtually normal memory of remote events preceding the onset of the amnestic syndrome, but are apt to display a profound disturbance in learning new material. Recently, Huppert and Piercy (*2*) have presented evidence suggesting that there may be at least two classes of the amnestic syndrome. In one, the formation of new memories is impaired, but retention over time of the newly formed memories is unimpaired. The second is characterized by an impairment (or no impairment) in the formation of new memories, but retention over time of the newly formed memories is impaired. Huppert and Piercy propose that the former type of amnesia is associated with diencephalic lesions, whereas the latter type is associated with hippocampal lesions.

The maze performance of adult male Wistar albino rats with either hippocampal or diencephalic lesions seems to extend Huppert and Piercy's dichotomization of the amnestic syndrome to lower mammalian forms (at least with respect to memory of spatial tasks) and provides further evidence for a dissociation between learning defects and retention defects in brain-damaged subjects. Control (normal and sham-operated) rats and rats prepared with dorsal hippocampal or medial mammillary body lesions (Fig. 1) were trained on a single-unit T-maze under the motive of escape-avoidance of footshock. On the day after preliminary training, each rat was required to choose the nonpreferred arm of the T (first reversal). On the next 3 days, each rat was trained to choose the arm of the T that had been incorrect on the immediately preceding day (reversals 2, 3, and 4). The correct arm led to an end box that could be entered by displacing an unlocked gray card. The incorrect arm, on the other hand, led to a locked gray card, which prevented the animal from entering the end box on that side. If the incorrect arm was chosen, the animal had to return to the choice point and choose the other arm of the T. An error (approach to within 7.5 cm of the locked gray card) was automatically punished by mild footshock. Training to the correct arm was continued until the animal reached the criterion of five consecutive errorless trials, the intertrial interval being held constant at 75 seconds. Each day the animal was given a test trial 5 minutes, 60 minutes, and 240 minutes after the criterion was met. During these three daily test trials of retention, the card on the incorrect side for that particular day was locked and punishment was given for errors.

A test trial of retention 24 hours after learning consisted of trial 1 on reversals 2, 3 and 4. Because the normal and sham-operated rats were virtually indistinguishable from each other in learning and retention scores, they were combined into one major control group for statistical purposes.

Both brain-damaged groups showed a learning defect; they were significantly inferior to the controls in mastering the four reversal problems (Table 1). While the animals with hippocampal lesions

Table 1. Mean learning errors per reversal, mean total errors on retention test trials, and fraction of subjects making at least one error on a given test trial.

Group	*N*	Learning errors	Retention errors	Fraction of subjects making errors			
				5 minutes	60 minutes	240 minutes	24 hours
Control	13	1.4	0	0	0	0	0
Hippocampus	8	6.9*	2.1*	1/8	4/8†	6/8†	2/8
Mammillary body	8	4.5*	0.5	1/8	1/8	0	2/8

*Significantly different from control group, $P < .05$ (Mann-Whitney U test). †Significantly different from control group, $P < .05$ (Fisher exact probability test).

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tended to be more impaired in reversal learning than those with mammillary body lesions, the difference in error scores was not statistically significant.

With respect to performance on the daily test trials, the hippocampal group (but not the mammillary-body group) showed a retention defect. None of the control animals made any errors on the 15 test trials. In contrast, six hippocampal animals and three mammillary body animals made at least one error on the 15 test trials. The difference in the proportion of animals making errors on test trials is significant (Fisher exact probability test, $P = .005$) for the hippocampal versus control group comparison, but not significant for the hippocampal versus mammillary body group comparison or the mammillary body versus control group comparison. However, the hippocampal group did make significantly more errors on test trials than did the mammillary body group (or the control group).

Analysis of performance at each test trial interval disclosed that the hippocampal group was significantly inferior to the control group at the 60- and 240-minute intervals, but not at the 5-minute or 24-hour interval. The mammillary body group was not significantly different from the control group at any one of the four intervals, but was significantly superior to the hippocampal group at the 240-minute interval ($P = .05$).

A reasonable explanation of these findings is that rats with hippocampal lesions tend to forget newly acquired spatial information faster than either control rats or rats with mammillary body lesions. A retrieval deficit seems unlikely since the hippocampal animals were comparable to the other two groups on the 5-minute retention test (*3*). Similarly, it cannot be argued that slow learners are necessarily fast "forgetters." The mammillary body group was impaired in learning the reversal problems but did not forget faster than the controls.

These results resemble those of Huppert and Piercy (*2*), who compared Korsakoff patients (with presumed diencephalic involvement) with H.M. (known to have hippocampal damage) and control subjects on a picture-recognition test. To adjust for differences in learning rates, the Korsakoff patients and H.M.

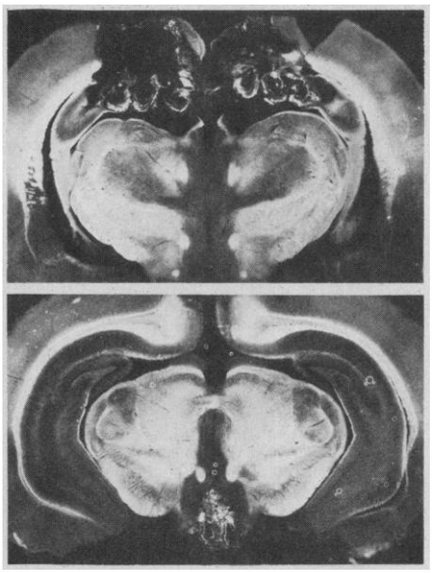

Fig. 1. Unstained sections showing representative lesions to the dorsal hippocampus (top) and medial mammillary bodies (bottom).

were allowed a longer inspection time for each picture than the controls. This procedure tended to equalize recognition scores achieved by the three groups on the 10-minute recognition test. When retested for retention 1 and 7 days later, the Korsakoff patients had a forgetting curve comparable to that of the controls, but H.M. forgot significantly faster than the other two groups. In like manner, the hippocampal, mammillary body, and control groups of our experiment were virtually equivalent in retention performance at the 5-minute test interval; yet the hippocampal animals forgot more rapidly than the other two groups at the 60- and 240-minute test intervals (*4*).

The contrast in performance between the hippocampal and mammillary body groups demonstrates a dissociation between learning defects and retention defects in brain-damaged animals. It seems, therefore, that experimentally induced "amnestic" states in animals may fall into at least two categories [(i) learning defect alone or (ii) retention defect, either alone or combined with a learning defect] in a manner similar to that shown by Huppert and Piercy for human patients with amnestic syndromes.

Highlighting further similarities with the data reported by Huppert and Piercy cannot seriously be defended. The amnestic syndrome in human patients with hippocampal (or diencephalic) lesions does not seem to be specific to the task; it is demonstrable in a variety of learning situations, such as picture recognition, maze performance, and story comprehension (*1*). In the rat, on the other hand, the memorial defects associated with hippocampal (and probably mammillary body) lesions are most reliably seen on spatial tasks (*5*).

Despite this major difference in performance between humans and rats having hippocampal damage, learning impairments in both groups may be, at least in part, expressions of a common dysfunction, namely, a defect in retention. In the rat, this defect may be restricted to spatial information. In the human, however, it seems to extend over a broad spectrum of learned activities.

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References and Notes

1. B. Milner, in *Biology of Memory*, K. H. Pribram and D. E. Broadbent, Eds. (Academic Press, New York, 1970); W. B. Scoville and B. Milner, *J. Neurol. Neurosurg. Psychiatry* **20**, 11 (1957); L. R. Squire and R. Y. Moore, *Ann. Neurol.* **6**, 503 (1979); G. A. Talland, *Deranged Memory* (Academic Press, New York, 1965); H. Victor, R. D. Adams, G. H. Collins, *The Wernicke Korsakoff Syndrome* (Davis, Philadelphia, 1971).
2. F. A. Huppert and M. Piercy, *Nature (London)* **275**, 317 (1978); *Cortex* **15**, 385 (1979).
3. I have replicated this effect in my laboratory. New groups of control rats ($N = 9$) and rats with hippocampal lesions ($N = 8$) were trained on four reversal problems. Only two daily test trials of retention (one at 5 minutes and one at 180 minutes after reaching the criterion) were given. No significant difference appeared at the 5-minute test interval (one hippocampal rat but no control rat making errors), but the difference at the 180-minute test interval was significant (five hippocampal rats but no control rat making errors) (Fisher exact probability test, $P = .01$).
4. The relatively high level of performance achieved by the hippocampal group at the 24-hour test interval is probably due to punishment for errors received during the 60-minute or 240-minute intervals, which would have the effect of strengthening the memory trace that weakened over time for the newly acquired spatial information. This explanation is supported by the results of the following experiment: The hippocampal and control groups described in (*3*) were trained on four additional reversal problems. This time, one reversal problem was given every 2 days. Before training the animals on reversals 2, 3, and 4 (and 2 days after learning reversal 4), a single test trial of retention was given. The mean response accuracy of control group was 86.1 percent on all four test trials, whereas that of the hippocampal group was only 65.8 percent (Mann-Whitney U test, $P = .01$).
5. J. O'Keefe and L. Nadel, *The Hippocampus as a Cognitive Map* (Clarendon, Oxford, 1978); D. S. Olton, *Sci. Am.* **236**, 82 (June 1977); J. Rosenstock, T. D. Field, E. Greene, *Exp. Neurol.* **55**, 340 (1977); R. Thompson, *Physiol. Psychol.* **2**, 1 (1974).

1 December 1980