suggest that the quinoline compounds contribute to the increased mortality of *P. americana* on high-protein diets.
17. Other species of cockroaches copulate for about 20 to 120 minutes. G. A. Parker [*Biol. Rev. Cambridge Philos. Soc.* **45**, 525 (1970)] suggests that long mating sequences may be a form of mate guarding (and paternity assurance) whereby the female is unavailable to other males when she is most receptive.
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Serial Position Curve in Rats: Role of the Dorsal Hippocampus

Abstract. *In an eight-arm radial maze, normal rats demonstrated good immediate retention for the order of first items (primacy component of serial position curve) and last items (recency component of serial position curve) of an eight-item (arm) list. In contrast, rats with dorsal hippocampal lesions displayed, on an immediate retention test, disruption of the primacy but not the recency component of the serial position curve. Furthermore, imposing a 10-minute delay before the retention test impaired all components of the serial position curve. These results support correspondence in mnemonic function of the hippocampus in animals and humans.*

The critical role of the hippocampus in the mediation of normal memory processes has been highlighted by the observation that in human patients bilateral damage to the medial temporal lobe, including the hippocampus, produces an extensive and durable amnesia for new information. The patients characteristically tend to forget daily events, have a relatively intact short-term memory (STM), but a deficient long-term memory (LTM) for specific events. Especially relevant to our experiment are the observations that amnesic patients with presumed hippocampal damage display (i) poor memory on an immediate test for the first items (primacy) of a list but excellent memory for the last items (recency) of the list, (ii) poor memory for all items of the list at a delayed test (*1*), and (iii) no apparent loss for general information relating to the rules for performing a particular task as long as specific information is available in STM (*2*).

We have observed in rats with hippocampal damage a pattern of memory deficits that parallels the human amnesic syndrome. In contrast to normal rats, who have good immediate memory for the order of presentation of the first and last items of a list of eight items (arms in a maze) and good memory only for the first, but not the last items, of the list at delayed retention tests, rats with dorsal hippocampal lesions have good immediate memory for the last, but not the first, items of the list, and have no memory for any of the items when retention tests are delayed. These data support the notion of correspondence in mnemonic function of the hippocampus in rats and humans and Iversen's hypothesis (*3*) that the correspondence was not previously observed because functionally equivalent tasks were not used. These data argue against the ideas that (i) the function of hippocampus is different for animals and humans, (ii) the amnesic syndrome produced by medial temporal lobe lesions is not due to hippocampal damage but rather is a function of damage to the temporal stem containing input and output pathways of temporal cortex and amygdala (*4*), and (iii) the amnesic syndrome is due not only to hippocampal damage but due to a combination of hippocampal plus amygdaloid damage (*5*).

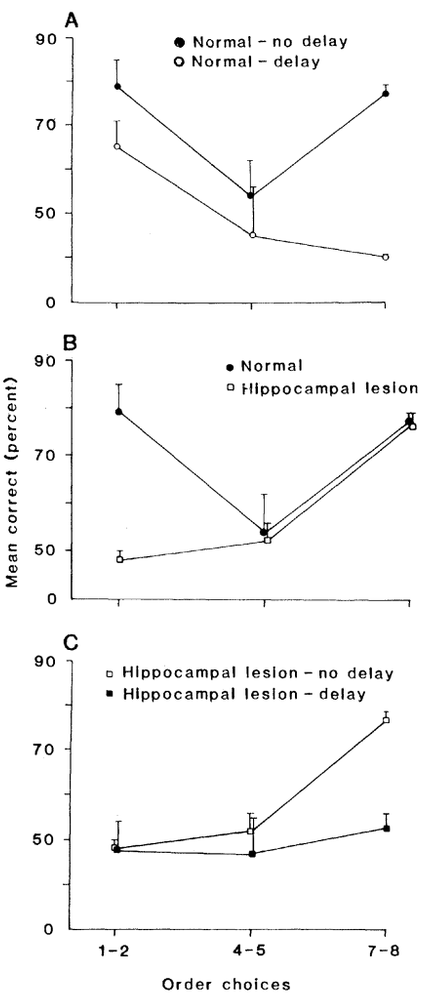

Fig. 1. (A) Serial position curve for normal subjects under no-delay (20-second) and delay (10-minute) conditions. (B) Serial position curve for normal and lesion states under an immediate retention test condition. (C) Serial position curve for subjects with hippocampal lesions under delay and no-delay conditions. I represents one standard error of the mean.

Four male Long-Evans rats 8 to 12 months old and weighing 360 to 480 g at the beginning of the experiment were studied. They were deprived of food to 80 percent of their free-feeding weight and allowed continuous access to water.

An elevated radial eight-arm maze similar to that described by Olton and Samuelson (*6*) was used with the addition of a set of clear Plexiglas doors that allowed the investigator to control access to any arm.

Animals were initially trained under the standard eight-arm procedure with all arms reinforced (*6*). Reinforcement consisted of small pieces of Froot Loops cereal. Once the animals were familiar with the apparatus and rapidly retrieved the food from each of the reinforced arms, they were switched to the serial list task. On each trial the animals were given access to the eight arms of the maze in a particular sequence and were tested 20 seconds later on their ability to discriminate which one of a given pair of arms was visited earlier in the sequence. The animals were first trained to a criterion of eight correct out of ten trials on a choice between the first and seventh arm in the sequence. This criterion was reached between 17 and 27 trials. After reaching criterion, each animal received at a 20-second delay on a random basis a choice (one test only) of either the first and second (1-2), fourth and fifth (4-5), or seventh and eighth (7-8) arms in the sequence. After 16 familiarization trials, each animal randomly received 12 trials for each 1-2, 4-5, and 7-8 position. All four rats displayed serial position effects, that is, prominent retention [better than chance (50 percent) performance] for 1-2 and 7-8 choice, but no retention (chance performance) for 4-5 choice (Fig. 1A). The same animals were then given 15 additional trials with five test trials for each 1-2, 4-5, and 7-8 choice but with the

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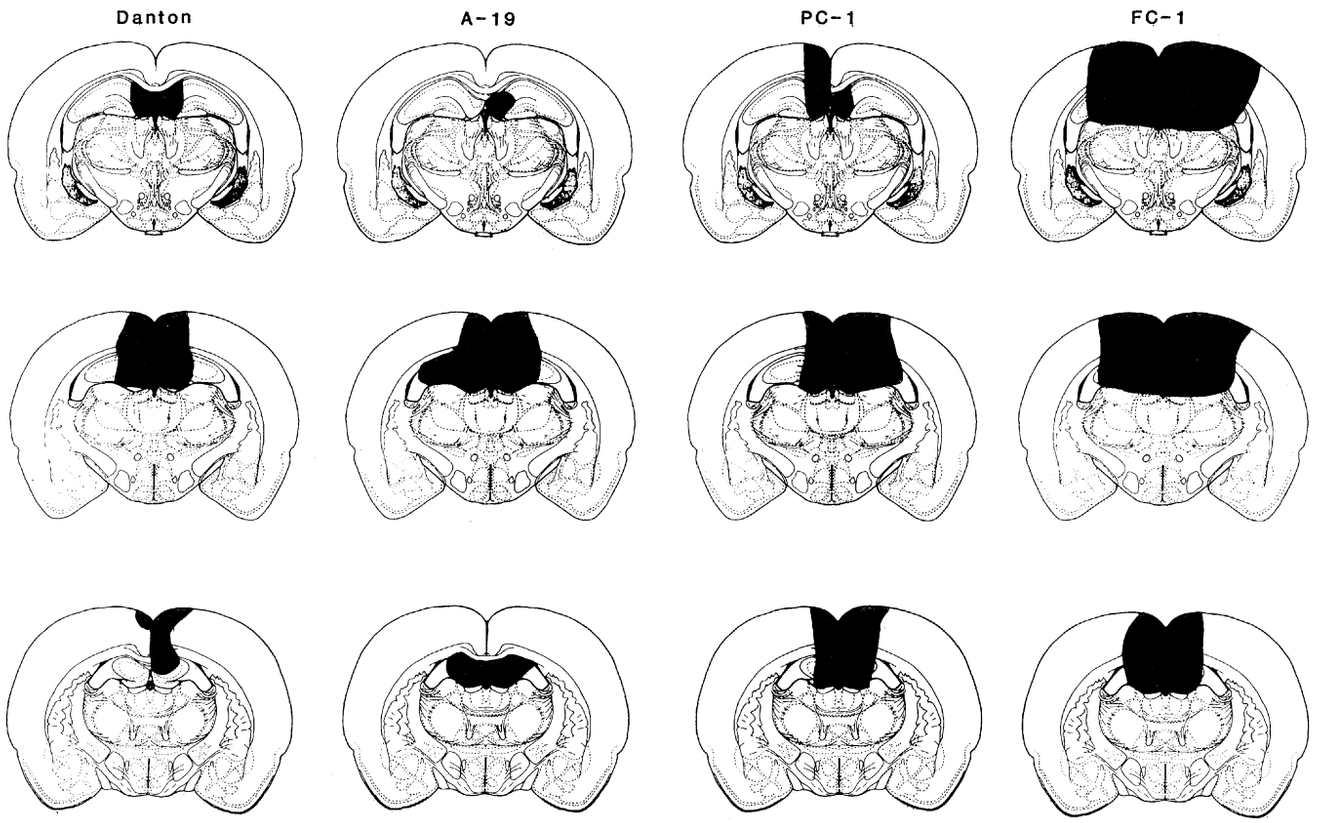

Fig. 2. Reconstructions of the brains of animals with hippocampal lesions. [Cross sections modified from (*12*)]

test delayed by 10 minutes. Retention of the 4-5 and 7-8 choice was at chance, while retention of 1-2 choice was still good (Fig. 1A) (*7*). Thus, a 10-minute delay disrupted the recency (7-8) portion of the serial position curve without markedly altering the primacy (1-2) component. To our knowledge, this is the first demonstration of a prominent serial position curve in rats.

Two animals received bilateral dorsal hippocampal lesions, and the others were subjected to sham operations. Since the sham operation had no deleterious effect on the animals' serial position performance, the two control animals were also given dorsal hippocampal lesions (*8*). All four animals were given 36 immediate tests with 12 at each choice position. Animals with lesions displayed excellent retention only for the 7-8 choice but none (chance performance) for the 1-2 choice (Fig. 1B) (*9*). Thus, in these animals the primacy (LTM), but not the recency (STM), component of the serial position curve was disrupted. All animals were then given 12 or 15 additional tests at a 10-minute delay. All animals performed at the chance level at all three choices, indicating that they had no memory for order information (Fig. 1C) (*10*).

The location and extent of the lesions for each animal are shown in Fig. 2 (*11*). Since all animals showed a loss in the primacy part of the curve, the animal with the smallest lesion (Danton) provides the most definitive information on the exact region in which damage causes the deficit. The dorsal hippocampus seems to be the critical region in mediating the primacy component of a serial position curve. Although Danton, as well as the others, sustained cortical damage in addition to the hippocampal damage, a control animal with only a cortical lesion did not display the deficits; therefore, it seems appropriate to assign the deficits to the hippocampal damage.

The performance of our animals resembled that of amnesic patients, including H.M., on memory for a list of items (*1*), in that hippocampal damage disrupted the primacy, but not the recency component of the serial position curve. Furthermore, akin to clinical descriptions of human amnesic patients, the rats with hippocampal lesions demonstrated no retention when an additional delay was included between the presentation and the retention test. Thus, it is possible to reproduce the most striking feature of the amnesic syndrome, namely a disruption of LTM, but not STM, for specific events in hippocampus-damaged rats.

An additional observation was that rats with lesions could remember the previously learned rule (choose the arm that occurred earlier in the sequence) given that the retention test required a choice between items 7 and 8 of the sequence. This result suggests that hippocampal damage did not interfere with the ability to remember the rule, but that the deficit in remembering items 1 and 2 of a particular sequence might have been due to incomplete encoding of the first two items. Similar results were obtained by Olton *et al.* (*2*), who studied animals with damage to the fimbria-fornix. In a 17-arm radial maze, they would repeatedly enter arms in which food was available (errors, related to working memory) but would not enter arms in which food was never available (no errors, related to reference memory). These studies, by inference from a parallel situation, provide some support for the contention that hippocampus-damaged rats, like humans, can remember rules while forgetting specific information. Our data provide support for a correspondence in mnemonic function of the hippocampus in animals and humans.

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7. An analysis of variance for two repeated measures (three choice orders by delay or no delay) (Fig. 1A) revealed a significant effect due to choice order [$F(1, 15) = 8.1$, $P < .01$], delay versus no delay [$F(1, 15) = 19.3$, $P < .001$], and choice order by delay interaction [$F(2, 15) = 3.5$, $P < .05$]. Subsequent Newman-Keuls tests indicated that (i) for the no-delay conditions, performance for the 1-2 and 7-8 choices was significantly better than that for the 4-5 choice ($P < .05$); (ii) for the delay condition, performance for 1-2 choice was significantly better than that for the 4-5 or 7-8 choice ($P < .05$); and (iii) only for the 7-8 choice was there a significant difference between delay and no-delay conditions ($P < .01$).
8. Under Nembutal anesthesia (45 mg per kilogram of body weight, injected intraperitoneally) animals received bilateral electrolytic lesions of the dorsal hippocampus. Insect pins (size 00) insulated with Epoxilite except for 1 mm at the tip were used as electrodes for making the lesions. Direct current (3 mA) was administered for 30 seconds with respect to a cathodal reference electrode in the rectum of the rat. Stereotaxic coordinates, based on a level skull between bregma and lambda and with depths relative to dura, were 4.0 mm posterior, ±1.4 and ±2.8 mm lateral, and 3.6 mm ventral. Animals were allowed 7 to 10 days recovery from surgery before testing was begun.
9. An analysis of variance for two repeated measures (three choice orders by lesion or normal) (Fig. 1B) revealed a significant effect due to choice order [$F(2, 15) = 18.2$, $P < .01$], lesions versus normal [$F(1, 15) = 11.9$, $P < .01$], and choice order by lesion interaction [$F(2, 15) = 9.7$, $P < .01$]. Subsequent Newman-Keuls tests indicated that (i) for the hippocampal lesion condition, performance for the 7-8 choice was significantly better than performance for the 4-5 or 1-2 choice ($P < .01$), and (ii) the hippocampal lesion condition was significantly different from normal only at the 1-2 choice ($P < .01$).
10. An analysis of variance for two repeated measures (three choice orders by delay or no delay) (Fig. 1C) revealed a significant effect due to choice order [$F(1, 15) = 6.5$, $P < .05$], delay versus no delay [$F(1, 15) = 15.8$, $P < .01$], and choice order by delay interaction [$F(2, 15) = 4.0$, $P < .05$]. Subsequent Newman-Keuls tests indicated that (i) for the no-delay conditions, performance for the 7-8 choice was significantly better than that for the 1-2 and 4-5 choice ($P < .01$), (ii) for the delay conditions there were no significant differences, and (iii) only for the 7-8 choice was there a significant difference between delay and no-delay conditions ($P < .01$).
11. At the end of the experiment, the animals were anesthetized with Nembutal, heparinized, and perfused intracardially with 10 percent Formalin in isotonic saline. Brains were excised, frozen, cut in 50-μm sections through the lesion, and stained with cresyl violet.
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Postural Asymmetry and Movement Disorder After Unilateral Microinjection of Adrenocorticotropin 1-24 in Rat Brainstem

Abstract. *A unilateral microinjection of adrenocorticotropin 1-24 in the rat brainstem in the region of the locus ceruleus resulted in postural asymmetry and movement disorder that resembled human dystonia, the severity and duration (2 to 3 days) being dose-dependent. These results show for the first time that neuropeptides in the brainstem may modulate posture and movement, and they suggest that some forms of movement disorder such as dystonia may be due to a disordered regulation of postural and locomotor mechanisms by adrenocorticotropin 1-24.*

The discovery of neuropeptides in the brain suggested the possibility that these substances may exert long-lasting neuromodulatory influences in the brain. However, the precise nature of the neurophysiological functions of these neurohormones remained to be elucidated. We report here for the first time that adrenocorticotropin (ACTH) 1-24 and shorter ACTH fragments exert potent and long-lasting (2 to 3 days) actions on posture and locomotion after direct administration in the rat brainstem. These results suggest that ACTH may participate in the tonic regulation of central programs that control posture and locomotion (*1*). Moreover, certain movement disorders such as dystonia (*2*) may be due to a disturbance in this regulation.

Adult male albino rats (300 to 350 g) were implanted under chloral hydrate (360 mg per kilogram of body weight) anesthesia with a single 30-gauge stainless steel cannula aimed at a site (with half of the rats in the left, the others in the right) 2 mm dorsal to the locus ceruleus (LC) (*3*). After 1 week to allow recovery from the surgery, the rats were microinjected with ACTH 1-24, ACTH 4-10, or α-melanocyte-stimulating hormone [α-MSH or (Ac–Ser^1, Val^{13}–NH_2, ACTH 1-13)] (Table 1); we used a needle prepared from 35-gauge stainless steel tubing [see (*4*) for details] that extended 2 mm beyond the guide tips into the region of the LC. Peptides dissolved in sterile 0.9 percent NaCl solution (and freshly prepared on each day of use) were injected in a volume of 1 μl at the rate of 0.1 μl per 15 seconds. After the microinjection, the rats were placed in individual transparent plastic bins (30 cm in diameter and 60 cm high) for observation.

Microinjection of ACTH 1-24 resulted in an immediate onset of a dose-dependent postural asymmetry and motor disorder (Fig. 1) that resembled the human movement disorder of dystonia. The postural asymmetry was invariably ipsilateral to the microinjection side; if the microinjection was into the left, the animal showed a left-leaning posture, and if into the right, a right-leaning posture. (Bilateral administrations of an equimolar dose of ACTH 1-24 resulted in retrocollis, an arching of the back.) This was accompanied by a disruption in normal locomotion such that when the animal attempted to move, it would wobble, topple over backward, or slowly rotate laterally in a creeping stance. However, when placed on a vertical grid, the animal showed strong grip on all four paws. Moreover, there was no paralysis; all limbs showed brisk withdrawal reflexes when noxious stimuli (pinches) were applied. The fact that the placing and reaching reflexes were unimpaired confirmed that there was no gross sensory deficit. Robust righting reflexes were present, with the animal resisting being placed on its back or being placed on the side contralateral to the microinjection side.

The syndrome we are describing here is distinctly different from the "catatonia" or "waxy flexibility" reported by Jacquet and Marks (*5*) after microinjection of β-endorphin in the rat periaqueductal gray; in these states, the rat could be molded into any position, however awkward, which the animal would then maintain for up to 1 hour. The syndrome reported here also differs from "barrel rotation," that is, brief (10-minute) episodes of rapid rotation along the longitudinal axis that was sometimes observed after intracerebral administrations of various neuropeptides (*6*). In some animals, these dystonic episodes were observed to last longer than 2 to 3 days. Mild stress (handling) appeared to exacerbate these episodes. In the acute phase of this episode, the animal often gave the appearance of being slowly pulled up on one side, with the result in some cases of toppling over backwards. As if to prevent such movements, the animals sometimes adopted the strategy of wedging themselves against the wall of the bin on the ipsilateral side (to the microinjection) so tightly that this resulted in the

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