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Long-Term Effects of Selective Neonatal Temporal Lobe Lesions on Learning and Memory in Monkeys

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Rhesus monkeys with neonatal damage to either the medial temporal lobe or the inferior temporal cortical area TE, and their normal controls, were reassessed in visual habit formation (24-hour intertrial interval task) and visual recognition (delayed nonmatching to sample; DNMS) at 4–5 years of age and then tested on tactile and spatial DNMS. Results on the two visual tasks were the same as those obtained when the monkeys were under 1 year of age. Specifically, early medial temporal lesions, like late lesions, left habit formation intact but severely impaired recognition memory. Furthermore, the memory deficit extended to the tactile and spatial modalities. By contrast, early damage to TE, unlike late damage to it, yielded only mild deficits on both visual tasks and had no effect on tactile or spatial DNMS. Compensatory mechanisms that promote substantial and permanent recovery thus appear to be available after neonatal TE lesions but not after neonatal medial temporal lesions.

Early damage to the medial temporal lobe in monkeys results in a visual recognition loss nearly as severe as that found after late damage to the same region (Bachevalier & Mishkin, 1994). This finding indicates that the medial temporal lobe operates early to sustain visual memory, that other regions cannot assume this function even when the damage occurs neonatally, and that recovery from early damage to this region is therefore limited at best. By contrast, early damage to the inferior temporal area TE, the last cortical area in the occipitotemporal pathway for modality-specific visual information processing, yielded only minimal impairment in visual recognition, as well as in visual discrimination habit formation (Bachevalier, Brickson, Hagger, & Mishkin, 1990; Bachevalier & Mishkin, 1994), both of which are severely impaired when the same damage occurs in adulthood (Mishkin & Phillips, 1990; Phillips, Malamut, Bachevalier, & Mishkin, 1988). These findings suggest that early area TE lesions, unlike early medial temporal removals, result in marked functional sparing, presumably because of the plasticity of other visual cortical areas, which can assume the functions of the damaged area (Webster, Bachevalier, & Ungerleider, 1994, 1995; Webster, Ungerleider, & Bachevalier, 1991a, 1991b).

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Whether functions are permanently lost or spared after early brain damage, however, depends on several factors besides the locus of injury and age at injury, including age at testing as well as the precise function measured (Goldman, 1971, 1974; Schneider, 1979). Thus, it remains possible that the evidence for sparing of functions after early area TE lesions and for loss of function after early medial temporal lesions, observed on certain tasks when the monkeys were still infants, might change with further maturation of the animals or with evaluation by other tests. For example, monkeys showing early functional preservation may in time show increasingly less sparing, or, conversely, those showing impairment initially may show eventual recovery (Goldman, 1971, 1974). To examine these possibilities in our monkeys with neonatal lesions, we retrained them in adulthood on the same visual tasks they had received as infants and also trained them on tactile and spatial memory tasks, which they had not received before.

Experiment 1

To assess the long-term effects of early medial temporal and inferior temporal lesions on visual learning and memory, the operated monkeys and their normal controls were retested at 4–5 years of age on concurrent object discrimination learning with 24-hr intertrial intervals (24-hr-ITI task, a test of habit formation) and then on a delayed nonmatching-to-sample task with trial-unique objects (DNMS, a test of recognition memory). The monkeys' scores on the two tasks were compared both with those they had obtained earlier as infants and with those obtained by monkeys that had received the same lesions in adulthood.

Method

Subjects

The subjects were 21 rhesus monkeys (*Macaca mulatta*) of both sexes, aged 4–5 years and weighing 3.75–6.5 kg at the beginning of the present study. Six monkeys (4 male and 2 female) had received

bilateral neonatal removals of the medial temporal lobe, including the amygdala, hippocampus, and underlying cortex (Group AH), 6 monkeys (2 male and 4 female) had received bilateral neonatal ablation of inferior temporal cortical area TE (Group TE), and the 9 remaining monkeys (4 male and 5 female) were unoperated controls (Group N).

A detailed description of their rearing conditions as infants and juveniles was given in an earlier report (Bachevalier et al., 1990). Briefly, all monkeys were born at the National Institutes of Health (NIH) Animal Center (Poolesville, Maryland) and raised in the primate nursery of the Laboratory of Neuropsychology (National Institute of Mental Health, Bethesda, Maryland). During their first year, they were tested on a series of cognitive tasks including preference for novelty at the ages of 5, 15, and 30 days (Bachevalier, Brickson, & Hagger, 1993), the 24-hr-ITI task at the age of 3 months (Bachevalier et al., 1990), and visual DNMS at the age of 10 months (Bachevalier & Mishkin, 1994). In addition, their social interactions with peers were measured at the ages of 2 and 6 months (Merjanian, Bachevalier, Pettigrew, & Mishkin, 1988), and their emotional reactions toward familiar and novel objects were evaluated at the age of 9 months (Nalwa & Bachevalier, 1991). From 1.5 to 2 years of age, they were moved to the NIH Animal Center, where they were first placed in groups of 3 to 6 monkeys for 1–2 years and then into individual cages until they reached 4–5 years of age. They were then returned to the Laboratory of Neuropsychology, where they were housed in individual cages and maintained on a diet of Purina Monkey Chow plus fresh fruit. Water was always available.

The monkeys given lesions when they were adults, with which the present animals were compared, were described in previous studies cited below.

Surgery

A detailed description of the neonatal surgical procedures is available in the initial report (Bachevalier et al., 1990). The lesions had been made in two stages—in one hemisphere when the monkeys were approximately 1 week of age and in the other when they were about 3 weeks of age. The bilateral medial temporal removals included the amygdala, periamygdaloid allocortex, hippocampal formation, and parahippocampal gyrus. Because the lesions extended laterally to the fundus of the rhinal sulcus, they included all entorhinal cortex. The bilateral removals of area TE extended ventrally from the fundus of the superior temporal sulcus to the lateral lip of the rhinal sulcus and fundus of the occipitotemporal sulcus, and anteriorly from a line approximately 9 mm rostral and parallel to the ascending portion of the inferior occipital sulcus to the temporal pole.

Lesion Assessment

The extent of each lesion was evaluated either histologically (TE-3, TE-5, TE-8) or by magnetic resonance (MR) imaging (TE-1, TE-4, TE-7, TE-8, and all cases with medial temporal lesions) and has already been reported (Bachevalier & Mishkin, 1994). For one case (TE-8), both types of analysis were available, each performed independently by a different observer. The nearly identical delineations of the extent of damage from histological sections and from MR images confirmed that aspiration lesions can be estimated precisely from MR images (Saunders, Aigner, & Frank, 1988). Coronal sections through two representative cases of each type of lesion are presented in Figure 1. Deviations from the intended lesions were minor.

In two of the medial temporal cases (AH-1 and AH-7), the caudalmost 1–2.5-mm portion of the hippocampus was spared bilaterally. In all cases, the lesion invaded the fundus of the rhinal sulcus along its entire length, thus encroaching on area 35 of the perirhinal cortex. In addition, at the caudal tip of the rhinal sulcus, the lesions included a small amount of perirhinal cortical area 36 (see Figure 1, AH-4 and AH-8, Level +10). As a result of mechanical and ischemic injury, there was unintended damage to the inferior temporal cortex unilaterally in four cases (AH-1, AH-2, AH-3, and AH-7) and bilaterally in two (see Figure 1, AH-4 and AH-8, Level 0). This damage was judged to be substantial only in Case AH-8, where it averaged 10% bilaterally of areas TE and TEO combined and also extended caudally on the ventromedial surface of the left hemisphere to include occipital cortex (see Figure 5 in Bachevalier & Mishkin, 1994).

As to deviations from the intended inferior temporal lesions, 1–2 mm of tissue lateral to the lateral lip of the rhinal sulcus was spared bilaterally in four cases (TE-1, TE-3, TE-7, and TE-8) and unilaterally in one (TE-4), thereby sparing almost all perirhinal cortical areas 36 and 35 in these instances (see Figure 1, Case TE-7 at Levels +17, +15, and +10; only at +20 did the lesion in this case invade area 36). In one of the TE cases (TE-5) only the rostral portion of the perirhinal cortex was spared bilaterally (see Figure 1, Case TE-5, Level +20). In three cases (TE-3, TE-5, and TE-8) the lesion encroached unilaterally on the most anterior portion of area TEO, the cortical visual area caudal to TE (see Figure 1, Case TE-5, Level 0 on the left).

Apparatus and Materials

Behavioral testing was carried out in a standard Wisconsin General Testing Apparatus (WGTA), which was located inside a darkened, sound-shielded room. Extraneous sound masking was provided by a white-noise generator. The test tray, which was located at the level of the floor of the monkey's transport cage, contained three food wells spaced 14 cm apart and aligned 12 cm in front of the cage. The test compartment was illuminated with a 60-W incandescent bulb, but the monkey's compartment was always unlit. The stimuli were junk objects that differed widely in shape, size, color, and texture. The food rewards were 300-mg banana pellets (P.J. Noyes, Lancaster, New Hampshire).

Procedure

The 24-hr-ITI task. Monkeys were trained to discriminate a set of 20 pairs of objects in the following way. For each pair, one object was arbitrarily designated as positive (i.e., baited with a food reward) and the other negative (i.e., unbaited). The baited and unbaited objects of the first pair were placed over the lateral wells of the test tray. After the monkey made a choice by displacing one of the objects, there was a 20-s interval following which the objects of the second pair were presented for choice, and this was repeated until all 20 pairs of objects had been presented once each. Twenty-four hours later, the same series of object-pairs was presented again. The positive and negative objects within each pair, as well as the order of the pairs, remained constant across sessions, but the left–right position of the objects in each pair was pseudorandomized daily. The set was presented once daily until the monkeys reached the criterion of 90 correct responses in 100 consecutive trials (i.e., 5 daily sessions). After completing one set, the monkeys were trained in the same way on a second set and, finally, on a third. A noncorrection technique was used throughout.

As already indicated, the scores obtained by the three groups of monkeys on the three sets (here labeled D, E, and F) were not only compared with each other but also used in two cross-study comparisons. For the first, the scores were compared with those the same monkeys had obtained as infants on three other sets (A, B, and C; Bachevalier et al., 1990). The testing procedures in the present experiment were the same as before except that the monkeys were now tested in a larger (standard-sized) WGTA and with larger objects than the ones used when they were infants, and they received the three sets in succession, whereas as infants they had received the first two sets for both learning and retention before receiving the third set for learning.

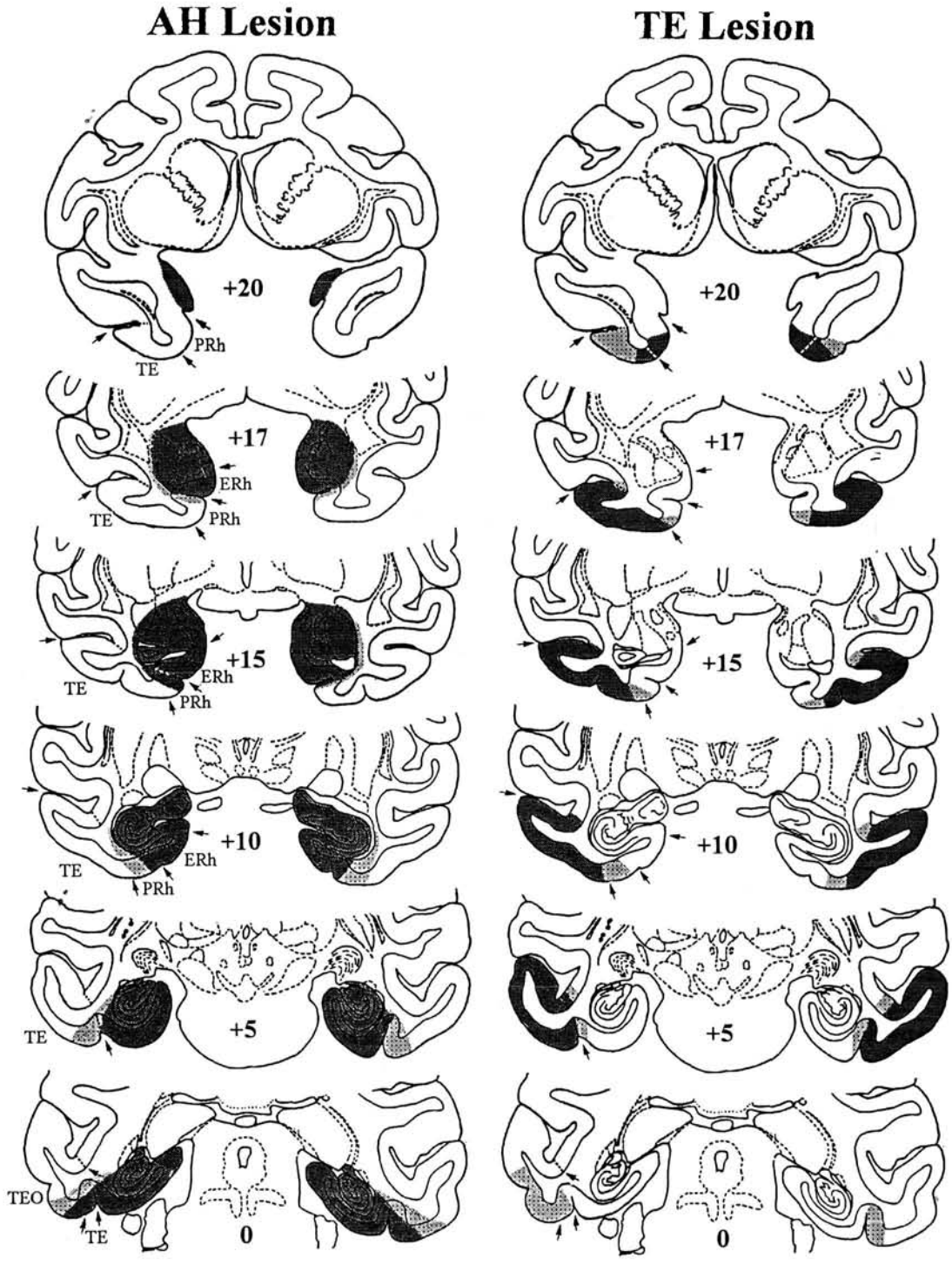

Figure 1. Coronal sections through the extent of damage in two representative cases with neonatal medial temporal lobe lesions (AH-4, dark gray, and AH-8, light gray) and inferior temporal lesions (TE-7, dark gray, and TE-5, light gray). Note that the extent of damage in AH-8 and TE-5 included both the dark and light gray areas with the following exceptions: in AH-8, Level +15, left hemisphere, the lesion ended ventrally at the fundus of the rhinal sulcus (white dashed line), and in TE-5, Level +20, both hemispheres, the lesion remained lateral to the rhinal sulcus (at white dashed line), thereby sparing the perirhinal cortex at those loci. Delineation of the entorhinal and perirhinal cortical fields follows the description of Meunier et al. (1993). Abbreviations: ERh = entorhinal cortex; PRh = perirhinal cortex; TE = inferior temporal cortical area TE; TEO = inferior temporal cortical area TEO.

(Also, sex differences in habit formation, examined when they were infants, were not examined here, because the number of male and female adult monkeys remaining in the two lesion groups was insufficient to allow statistical comparison.)

For the second cross-study comparison, the results of the present experiment were compared with the results described in Malamut, Saunders, and Mishkin (1984) and Phillips et al. (1988) for animals that had received medial temporal and inferior temporal lesions, respectively, when they were already mature.

Visual DNMS. At least 2 weeks after attaining criterion on the last set of objects in the 24-hr-ITI task, the monkeys were trained on visual DNMS with trial-unique objects. In this task, each trial consisted of two parts. First, a sample object was presented over the central well of the test tray, which the monkey uncovered to retrieve the food reward. After a 10-s delay, the same object was presented again together with a new object, each over a lateral well. In this choice test, the reward was located under the new object, its left–right position having been pseudorandomized. After a 30-s intertrial interval, another trial was given in the same way but with a new pair of objects, and this was repeated for 20 daily trials. Testing continued in this manner until the monkey reached a criterion of 90 correct responses in 100 consecutive trials. A noncorrection technique was used throughout. The objects were chosen from a pool of approximately 2,000 objects. Once an object had been used, it was set aside until all the other objects of the pool had been presented, and so it did not reappear for about 10 weeks.

Following a 2-week rest period, the monkeys were retrained on visual DNMS to criterion and then given a performance test as follows. First, the delay between the sample presentation and the choice test was progressively increased from 10 s to 30, 60, and finally 120 s, and then the list of objects to be remembered was increased in stages from 1 object to 3, 5, and finally 10 objects. Monkeys were tested for 100 trials at each delay (20 trials per session for 5 consecutive days) and 150 trials at each list length (30 trials per session for 5 consecutive days). In the list-length tests, the samples were presented successively at 20-s intervals, followed by choice tests also at 20-s intervals. Consequently, the minimum delay between the familiarization phase and the choice test was 60 s, 100 s, and 200 s for lists of 3, 5, and 10 objects, respectively.

Again, the learning and performance scores of the monkeys were compared first with those they had obtained when they were tested on the same task at 10 months of age. Then performance scores but not learning scores were compared with those obtained by monkeys that had received the same medial temporal lesions (Mishkin, 1978) or area TE lesions (Mishkin & Phillips, 1990) in adulthood. (The learning scores of the two groups were not compared because of different amounts of training in the DNMS rule that they had received.) Testing procedures used for the two age groups were the same, except, as already indicated, both the WGTA and the objects were larger for the adult monkeys than for the infants.

Results and Discussion

The 24-hr-ITI Task

The number of sessions and errors each monkey required to reach the criterion in Sets D, E, and F are given in Table 1. A Lesion × Set analysis of variance with repeated measures for the last factor indicated a significant effect of lesion, $F(2, 18) = 10.10$, $p < .001$, and $F(2, 18) = 12.39$, $p < .001$, for sessions and errors, respectively, but not of sets or of the interaction between lesion and sets. Paired comparisons (Tukey) indicated that Group TE required more training to reach criterion than both Group N ($p < .001$ for sessions and errors) and Group AH ($p < .06$ for sessions and $p < .025$ for errors), whereas the latter two groups did not differ from each other.

Table 1
Concurrent Visual Discrimination Learning (24-hr-ITI Task)

		Set D		Set E		Set F	
Group/case	Sex	S	E	S	E	S	E
N							
N-2	F	10	65	8	48	7	37
N-3	F	6	49	5	32	4	34
N-6	F	10	54	10	65	6	32
N-13	F	10	68	11	88	5	20
N-15	F	6	45	4	38	2	18
N-1	M	8	66	6	40	3	24
N-8	M	6	44	10	75	5	35
N-11	M	4	31	6	47	4	24
N-14	M	6	39	6	41	7	44
M		7	51	7	53	5	30
TE							
TE-1	F	11	76	12	89	9	53
TE-3	F	14	91	9	75	9	61
TE-5	F	18	104	20	105	12	69
TE-8	F	13	93	7	51	7	40
TE-4	M	18	131	9	79	9	57
TE-7	M	14	78	26	187	25	160
M		15	96	14	98	12	73
AH							
AH-1	F	10	69	6	43	9	45
AH-3	F	11	60	6	56	17	114
AH-2	M	10	58	6	55	12	82
AH-4	M	7	58	8	49	7	48
AH-7	M	10	61	11	69	13	70
AH-8	M	11	65	7	45	6	44
M		10	62	7	53	11	67

Note. ITI = intertrial interval. Scores are number of daily sessions, S, and total number of errors, E, before attainment of criterion on Sets D, E, and F when animals were 4–5 years of age. Group N = normal controls, Group TE = monkeys with neonatal inferior temporal lesions, Group AH = monkeys with neonatal medial temporal lesions. F = female, M = male.

As reported earlier (Bachevalier et al., 1990), the scores of infant monkeys in all three groups improved markedly from Set A to Sets B and C (see Figure 2). Therefore, to examine the effect of age at testing, the average scores across Sets B and C were compared with the average scores across Sets D, E, and F by an analysis of variance, with the factors being lesion and age at testing as a repeated measure. Again, the effect of lesion was significant, $F(2, 11) = 13.03$, $p < .001$, and $F(2, 11) = 18.07$, $p < .001$, for sessions and errors, respectively, but there was no effect of age and no Lesion × Age interaction, suggesting that performance on this task did not change across age in any of the groups. Paired comparisons performed on the lesion factor indicated that Group TE required significantly more trials and made more errors than both Group N and Group AH (all $ps < .05$).

Finally, the average scores across Sets D, E, and F were compared with the average scores across Sets A, B, and C of monkeys that had received either medial temporal or area TE lesions in adulthood (Malamut et al., 1984 and Phillips et al., 1988; two monkeys with TE lesions in the latter study that had

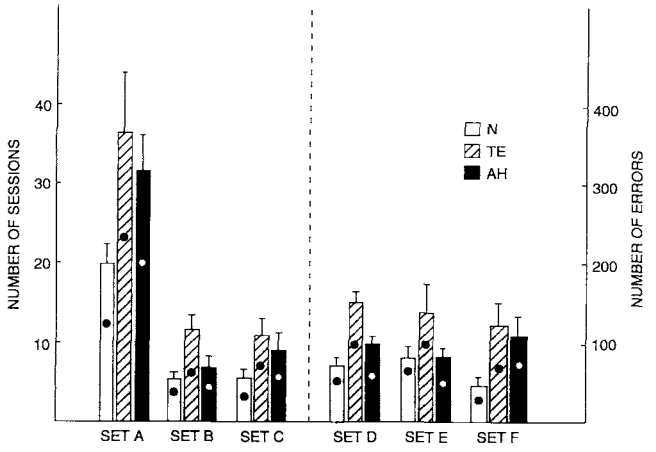

Figure 2. Average number (+*SEM*) of sessions to criterion for the three sets of discriminations at 3 months of age (Sets A, B, and C) and at 4–5 years of age (Sets D, E, and F). Seven monkeys that had been tested in infancy only on Sets A and B have been excluded. Infant data from Bachevalier et al. (1990). Group N = normal controls, Group TE = monkeys with neonatal inferior temporal lesions, and Group AH = monkeys with neonatal medial temporal lesions. Circles are average number of errors to criterion.

failed to reach criterion within the limits of testing were excluded from the analysis; see Figure 3). A Lesion × Age at Lesion (neonatal vs. adult) analysis of variance revealed significant effects of both lesion, $F(2, 31) = 41.78, p < .001$, and $F(2, 31) = 40.62, p < .001$, for sessions and errors, respectively, and age, $F(1, 31) = 27.52, p < .001$, and $F(1, 31) = 19.40, p < .001$, for sessions and errors, respectively, as well as of the interactions between these two factors, $F(2, 31) = 5.87, p < .01$, and $F(2, 31) = 4.31, p < .02$, for sessions and errors, respectively. Paired comparisons (Bonferroni) indicated that neither the two medial temporal groups nor the two normal control groups differed significantly. By contrast, the monkeys with neonatal area TE lesions learned the task significantly faster than those that had received the same lesions in adulthood ($t = 5.81, p < .001$, and $t = 4.92, p < .001$, for trials and errors, respectively).

Visual DNMS

Relearning and retention. Because the monkeys had learned the DNMS rule as infants, their scores in the present experiment may be considered relearning scores. The number of trials and errors each monkey required to relearn and, 2 weeks later, retain visual DNMS is shown in Table 2. Because several monkeys obtained scores of zero trials and errors both to relearn and to retain the DNMS rule, the data were analyzed by a nonparametric Kruskal-Wallis one-way analysis of variance. The analysis of the relearning scores showed a significant effect of lesion, $H(2) = 15.49, p < .001$, and $H(2) = 16.06, p < .001$, for trials and errors, respectively. Paired comparisons indicated that both Group TE and Group AH required more trials, $U(1) = .50, p < .002$, and $U(1) = 0, p < .001$, for TE versus N and AH versus N, respectively, and made more errors, $U(1) = 0, p < .001$, and $U(1) = 0, p < .001$, than Group N. In addition, the difference between Groups AH and TE was nearly significant for errors, $U(1) = 6.00, p < .055$, but not for trials.

All monkeys showed good retention of the DNMS rule after 2 weeks, requiring fewer trials to reach criterion than they had taken in relearning. The effect of lesion in retention was not significant.

To assess the effect of age at testing, the monkeys' scores were compared with those they had obtained earlier, at 10 months of age (Bachevalier & Mishkin, 1994; see Figure 4). Infant and adult scores were compared by a nonparametric Friedman one-way analysis of variance for each lesion group separately. Both Group N and Group TE required significantly fewer trials and made fewer errors to relearn the DNMS rule than they had taken originally to learn it in infancy: Group N, $H(1) = 9.0, p < .003$, and $H(1) = 0, p < .003$, for trials and errors, respectively; Group TE, $H(1) = 6.0, p < .02$, and $H(1) = 6.0, p < .02$, for trials and errors, respectively. By contrast, the difference was not significant in Group AH, which required about the same amount of training to relearn the task in adulthood as it had needed in infancy. At both ages, all groups showed good retention of the DNMS rule when retested 2 weeks after first attaining criterion, and there was no age difference in this measure in any group.

Performance test. Scores obtained by each monkey on the 6 conditions of the performance test are given in Table 3 and Figure 5. A Lesion × Condition analysis of variance with

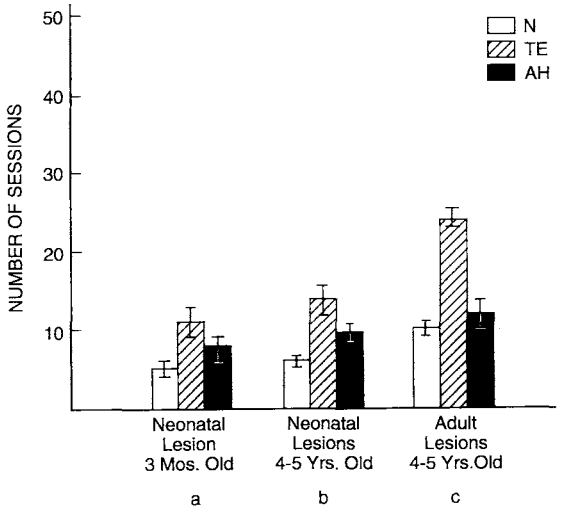

Figure 3. Concurrent visual discrimination learning. a. Average number (+*SEM*) of sessions to criterion across Sets B and C in monkeys with neonatal lesions and their normal controls tested at the age of 3 months. b. Average number (+*SEM*) of sessions to criterion across Sets D, E, and F in monkeys with neonatal lesions and their normal controls tested at the age of 4–5 years. In a and b, only those monkeys that had completed all three sets as infants are included. c. Average number (+*SEM*) of sessions to criterion on Sets A, B, and C in monkeys with lesions sustained as adults and their normal controls (from Malamut et al., 1984, and Phillips et al., 1988). N = normal controls, TE = groups with inferior temporal lesions, and AH = groups with medial temporal lesions.

Table 2
Visual Delayed Nonmatching-to-Sample Task

Group/case	Sex	Relearning T	Relearning E	Retention T	Retention E	%
N						
N-2	F	40	7	0	0	95
N-3	F	0	0	20	6	94
N-6	F	20	3	0	0	94
N-13	F	0	0	0	0	92
N-15	F	40	11	0	0	96
N-1	M	20	7	0	0	99
N-8	M	60	7	0	0	98
N-11	M	40	12	0	0	91
N-14	M	0	0	0	0	97
M		24	5	2	1	95
TE						
TE-1	F	180	47	0	0	91
TE-3	F	60	13	0	0	93
TE-5	F	180	64	100	24	92
TE-8	F	80	26	0	0	91
TE-4	M	240	54	80	17	91
TE-7	M	220	75	0	0	90
M		160	47	30	7	91
AH						
AH-1	F	600	130	220	48	92
AH-3	F	360	67	220	38	91
AH-2	M	120	68	20	3	90
AH-4	M	760	210	0	0	92
AH-7	M	120	43	0	0	92
AH-8	M	640	171	80	13	92
M		433	115	90	17	92

Note. Scores are number of trials, T, and total number of errors, E, preceding criterion when animals were 4–5 years of age. % represents percentage correct responses during criterion (last 100 trials). Group N = normal controls, Group TE = monkeys with neonatal inferior temporal lesions, Group AH = monkeys with neonatal medial temporal lesions, F = female, M = male.

repeated measures revealed significant main effects of lesion, $F(2, 18) = 33.81, p < .001$, and condition, $F(2, 35) = 52.38$, $p < .001$. Paired comparisons indicated that both Groups TE and AH performed significantly worse than Group N and also that Group AH performed significantly worse than Group TE (all *p*s [.01). In addition, there was a significant interaction between lesion and condition, F(Greenhouse-Geisser 4, 35) = 4.76, $p < .003$, indicating that the scores of both operated groups fell disproportionately with increasing memory demands. In fact, this was the case for both Groups AH and TE, since omission of either one from the statistical analysis did not eliminate the interaction, F(Greenhouse-Geisser 3, 39) = 6.20, $p < .001$, and F(Greenhouse-Geisser 3, 39) = 5.54, $p < .002$, after omitting Groups AH and TE, respectively. Yet, the pattern as well as degree of deficit following the two lesions was clearly different. The mean scores of Group TE (88%) were similar to those of Group N (93%) across the three delays, although they were lower (74%) than those of Group N (86%) across the three list lengths. Group AH, by contrast, performed more poorly on both measures (74% on the delays and 62% on the list lengths). Separate analyses of variance on the delay and list length tests yielded significant effects of lesion on both, $F(2, 18) = 26.21, p < .0001$, and $F(2, 18) = 29.79, p < .0001$, respectively. Paired comparisons showed that Group AH performed more poorly than both Groups N and TE on both delays and lists, whereas Group TE fell significantly below Group N on lists only.

To assess the effect of age at testing on the monkeys' performance, a Lesion × Condition × Age analysis of variance with repeated measures for the last two factors was performed, comparing the present scores with those the monkeys obtained when they were tested as infants (Bachevalier & Mishkin, 1994). The analysis revealed that the three main effects were significant, $F(2, 18) = 49.44, p < .001$, F(Greenhouse-Geisser 4, 65) = 22.77, $p < .001$, and $F(1, 18) = 217.92, p < .001$, for lesion, condition, and age, respectively, as were the interactions between lesion and age, $F(2, 18) = 32.09$, $p < .001$, condition and age, F(Greenhouse-Geisser 4, 66), = 4.09, $p < .002$, and lesion, condition, and age, F(Greenhouse-Geisser 7, 66) = 4.03, $p < 0.001$. Paired comparisons (Tukey) performed on the lesion factor indicated that although Group TE performed more poorly than Group N, Group AH performed more poorly than both (all *p*s $< .05$). In addition, the Lesion × Condition × Age interaction revealed that although all monkeys performed slightly more poorly in adulthood than in infancy, this decrease in performance was significant for Group TE only on the delay condition, for Group AH only on the list condition, but not for Group N on either condition.

Finally, the average scores across the six delay and list conditions were compared with the average scores of monkeys that had received the same lesions as adults (Mishkin, 1978; Mishkin & Phillips, 1990; see Figure 6). A Lesion × Age (neonatal vs. adult lesion) analysis of variance indicated a significant effect of both lesion, $F(2, 24) = 85.32, p < .001$, and age, $F(1, 24) = 10.11, p < .004$, and of their interaction, $F(2,$

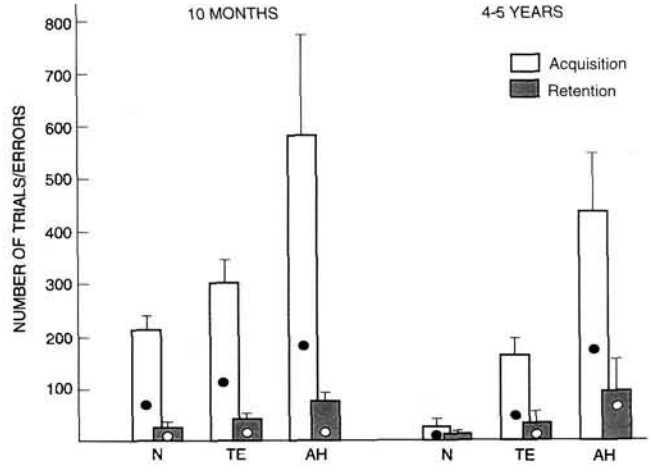

Figure 4. Average number of trials (+*SEM*) to criterion on learning or relearning (white bars) and retention (gray bars) of visual delayed nonmatching-to-sample task in monkeys tested at 10 months of age and at 4–5 years of age. Circles indicate average number of errors to criterion. Infant data from Bachevalier and Mishkin (1994). Group N = normal controls, Group TE = monkeys with neonatal inferior temporal lesions, and Group AH = monkeys with neonatal medial temporal lesions.

Table 3
Visual Delayed Nonmatching-to-Sample Performance Test

Group/case	Sex	Delay			List length			AVG
		30 s	60 s	120 s	3	5	10	
N								
N-2	F	96	95	92	92	88	80	90.8
N-3	F	92	89	87	90	82	66	84.5
N-6	F	82	83	82	81	84	60	78.8
N-13	F	89	95	94	91	90	83	90.3
N-15	F	96	99	96	94	83	80	91.4
N-1	M	96	96	97	98	98	92	96.2
N-8	M	96	96	94	89	88	77	90.0
N-11	M	96	99	97	92	94	83	93.7
N-14	M	94	91	93	92	89	79	89.6
M		93	93	92	91	88	78	89.5
TE								
TE-1	F	88	81	84	76	65	55	74.8
TE-3	F	91	90	87	85	77	71	83.5
TE-5	F	92	77	81	74	60	59	74.0
TE-8	F	95	93	95	94	82	71	88.5
TE-4	M	88	81	82	79	80	64	79.3
TE-7	M	91	90	93	82	74	75	84.4
M		91	85	87	82	73	66	80.75
AH								
AH-1	F	81	79	74	62	64	70	72.0
AH-3	F	83	73	61	57	60	63	66.2
AH-2	M	75	66	66	66	71	59	67.3
AH-4	M	76	81	66	58	56	53	65.3
AH-7	M	73	68	57	69	63	56	64.6
AH-8	M	87	75	86	65	60	67	73.4
M		79	74	68	63	62	61	68.3

Note. Scores are percentage of correct responses in 100 trials at each delay interval and 150 trials at each list length when animals were tested as adults at 4–5 years of age. AVG denotes average across the six conditions of the performance test. Group N = normal controls, Group TE = monkeys with neonatal inferior temporal lesions, Group AH = monkeys with neonatal medial temporal lesions, F = female, M = male.

24) = 13.54, $p < .001$. Paired comparisons (Bonferroni) showed that neither the two medial temporal groups nor the two normal control groups differed significantly. By contrast, the group given TE lesions neonatally performed significantly better than the one that had received the same lesions in adulthood ($t = 4.91, p < .001$).

Comment

In summary, neonatal medial temporal lesions left visual habit formation intact at both test ages. This negative finding corroborates the negative result obtained originally in the monkeys given such lesions when they were adults (Malamut et al., 1984), indicating that medial temporal lobe structures are not involved in the circuitry mediating visual habit formation. By contrast, the same monkeys with neonatal medial temporal lesions showed a severe visual recognition loss at both test ages. Their scores on the performance test did not change appreciably between infancy and adulthood, except for a small but significant drop (2%) in the list conditions. Furthermore, although the absolute level of their performance was higher than that of the monkeys given the same lesions in adulthood, the difference was not statistically significant.

A different pattern of results was obtained in the monkeys with neonatal inferior temporal lesions, namely a mild impairment in both visual habit formation and visual recognition at both ages of testing. Indeed, the impairment in recognition appeared only on the list conditions, even though their average performance across delays dropped slightly but significantly (3%) from infancy to adulthood. Furthermore, their impairments on both tests at both ages were significantly less than those of the monkeys given the same lesions as adults. It was found recently (M. J. Webster, personal communication, August 18, 1994) that the visual recognition loss seen initially postoperatively in monkeys given inferior temporal lesions in adulthood remains severe for at least 2 years after surgery. Clearly, the substantial sparing of both visual habit and visual memory functions found here after neonatal inferior temporal lesions is at least as long lasting.

Experiment 2

In addition to their severe visual recognition impairment, monkeys given medial temporal lesions in adulthood are profoundly impaired in recognizing objects by touch as well as in recalling spatial locations, indicating that their amnesia is global in nature (Angeli, Murray, & Mishkin, 1993; Murray & Mishkin, 1984; Parkinson, Murray, & Mishkin, 1988). This pattern contrasts with that following damage to area TE in

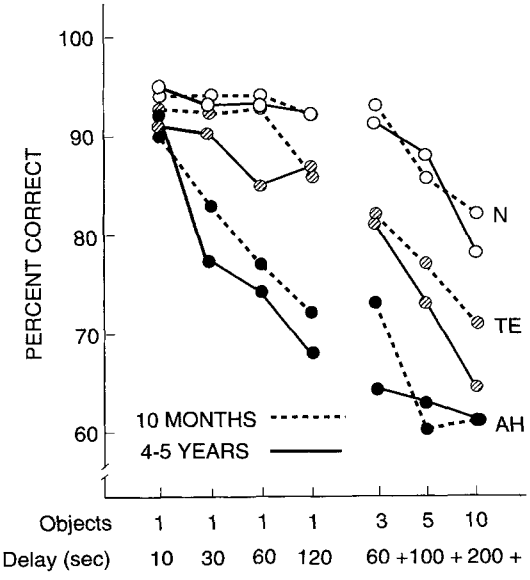

Figure 5. Average scores on the performance test in monkeys tested at 10 months of age (dashed line) and at 4–5 years of age (solid line). The first point of the curve indicates the average final score achieved on relearning the basic task, which entailed recognizing single objects after 10 s; monkeys were tested on the six remaining conditions, involving gradually increasing delays and list lengths, for 1 week each. Infant data from Bachevalier and Mishkin (1994). Group N = normal controls, Group TE = monkeys with neonatal inferior temporal lesions, and Group AH = monkeys with neonatal medial temporal lesions.

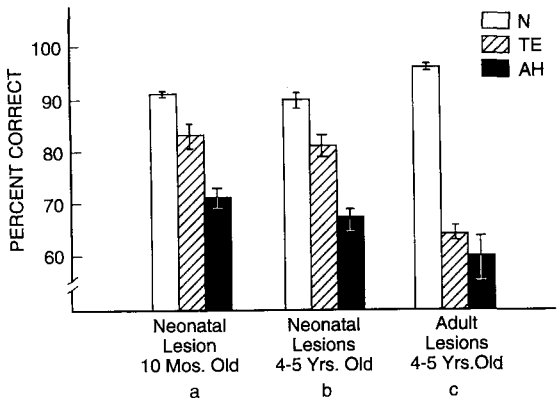

Figure 6. Performance on visual delayed nonmatching to sample. a. Average percentage of correct responses (+*SEM*) across the three longer delays (30, 60, and 120 s) and the three list lengths (3, 5, and 10) in monkeys with neonatal lesions and their normal controls tested as infants at 10 months of age. b. Average percentage of correct responses (+*SEM*) across the delays and the list lengths in monkeys with neonatal lesions and their normal controls tested as adults at 4–5 years of age. c. Average percentage of correct responses (+*SEM*) across the delays and the list lengths in monkeys with lesions sustained as adults (from Mishkin, 1978, and Mishkin & Phillips, 1990). N = normal controls, TE = groups with inferior temporal lesions, and AH = groups with medial temporal lesions.

adult monkeys, who show a selective visual disorder, that is, one that affects visual discrimination learning and visual recognition but not tactile recognition (Pons, Murray, & Mishkin, 1989) or spatial memory (Mishkin, 1954). To determine whether the same dissociation holds for the effects of neonatal lesions, we tested the monkeys in both a tactile and a spatial delayed nonmatching-to-sample task. To assure that any tactile impairment that was found reflected a genuine memory loss and not simply a difficulty in distinguishing objects by touch, a tactile discrimination learning task was added as a control measure.

Method

Subjects

The subjects were 15 of the rhesus monkeys (*Macaca mulatta*) that had served in Experiment 1. There were 6 monkeys (N-2, N-3, N-6, N-8, N-11, and N-14) from Group N, 4 monkeys (TE-1, TE-4, TE-7, and TE-8) from Group TE, and 5 monkeys (AH-1, AH-2, AH-3, AH-4, and AH-7) from Group AH.

Apparatus and Materials

All testing was conducted in the WGTA under the same general conditions as in the first experiment. For the tactile tasks, the WGTA was modified slightly to allow testing of the monkeys in the dark, as described previously by Murray and Mishkin (1984). For this purpose, the 60-W incandescent bulb of the test compartment was illuminated only in the pretraining phases, during which it was first fully lit and then progressively dimmed by use of a variable resistor. The animal compartment of the WGTA was always unlit, and the one-way vision screen through which the animal's test behavior was normally observed was replaced by an opaque screen. The monkey's behavior in the dark was monitored on a video screen linked to an infrared camera, which, together with an infrared light source, was mounted over the test compartment. The test tray, painted black, contained a row of three food wells spaced 15 cm apart, center to center. Light-emitting diodes (LEDs), recessed in the test tray 4.5 cm in front of each well, were used to signal the position of the objects during tactual testing, but they did not provide sufficient light for visual inspection of the objects.

The monkeys were trained with a fixed set of 50 objects that differed widely in shape, size, texture, and compressibility, so that each would be tactually distinctive. Each object was mounted on a cork base, which fitted tightly into the wells of the testing board. Large banana pellets (P. J. Noyes, 500 mg) were used as rewards to ensure their easy retrieval in complete darkness.

For spatial DNMS, the test compartment was illuminated and the one-way vision screen was replaced. The test tray contained nine wells, distributed in three rows of three wells each (10 cm apart, center to center). Two identical gray plaques (5 × 5 cm) were used to cover the wells on each trial, and the smaller banana pellets (P. J. Noyes, 300 mg) again served as rewards.

Procedure

Tactile DNMS. Training on tactile DNMS was started approximately 1 year after all monkeys had completed visual DNMS. As in the visual version of the task, each trial consisted of two phases. In the familiarization phase, the monkey was presented with a baited sample object covering the central well. Ten seconds later, the monkey was presented with a choice between the sample object and a new object, both covering the lateral wells, and the monkey was rewarded for choosing the new object. After 30 s, a new trial began with a new pair of objects, and so on for 20 trials per day. No object was used more than once in each daily session, and the objects were randomly re-paired each day. The left–right position of the baited objects during the choice test was counterbalanced pseudorandomly.

Before formal testing on the tactile DNMS began, the monkeys were pretrained as follows. In Phase 1, the test compartment was fully illuminated and the cork-mounted objects were inserted in the wells only partly, and at an angle, so that the monkeys could displace them easily. As training progressed, the cork-mounted objects were inserted more deeply into the wells, forcing the monkey to grasp them firmly in order to remove them and obtain the food reward. This phase ended when the monkey removed the fully inserted objects without hesitation. In Phase 2, the light in the test compartment was dimmed progressively until the monkey performed the task in complete darkness. Finally, in Phase 3, also conducted in complete darkness, each incorrect choice was followed by a correction procedure, which consisted of repeated re-presentation of the entire trial sequence (sample presentation plus choice test) until the monkey chose correctly. This procedure was continued until the monkey spontaneously compared the two objects tactilely on at least five trials each day for 2 consecutive days before making a choice. Following the three pretraining phases, formal scoring began, with testing continuing without correction until the monkey reached the criterion of 90 correct choices in 100 trials distributed across 5 consecutive days. Monkeys that did not reach criterion within 1,000 trials were given 500 additional trials with a correction procedure in which an error was followed by unscored re-presentations of the choice test only, until the monkey responded correctly. After reaching criterion, or on completion of the 500 correction trials, the monkeys were given a performance test in which the delay between sample presentation and choice was increased from 10 s to 30, 60, and finally 120 s. They were tested for 100 trials at each delay (20 trials per session for 5 consecutive days).

Tactile discrimination. All monkeys except N-2, N-6, and TE-8 were given a standard tactile discrimination problem in which two objects, one baited and one unbaited, were presented by the noncorrection technique for 30 trials per day. The left–right position of the positive object was determined pseudorandomly, and the trials were separated by 20-s intervals. The monkeys were trained until they reached the criterion of 90% correct responses in one session. A second pair of objects was then introduced, and the monkeys were tested to the same criterion and in the same manner as for the first pair.

Spatial DNMS. Two weeks after completion of the tactile discrimination task, all monkeys except TE-8 were tested in spatial DNMS, using a modified version of a task previously described by Mahut and Moss (1986). As in DNMS presented in the visual or tactile mode, each trial of the DNMS for locations consisted of two phases (Figure 7). For sample presentation, one baited well (sample) was covered with a

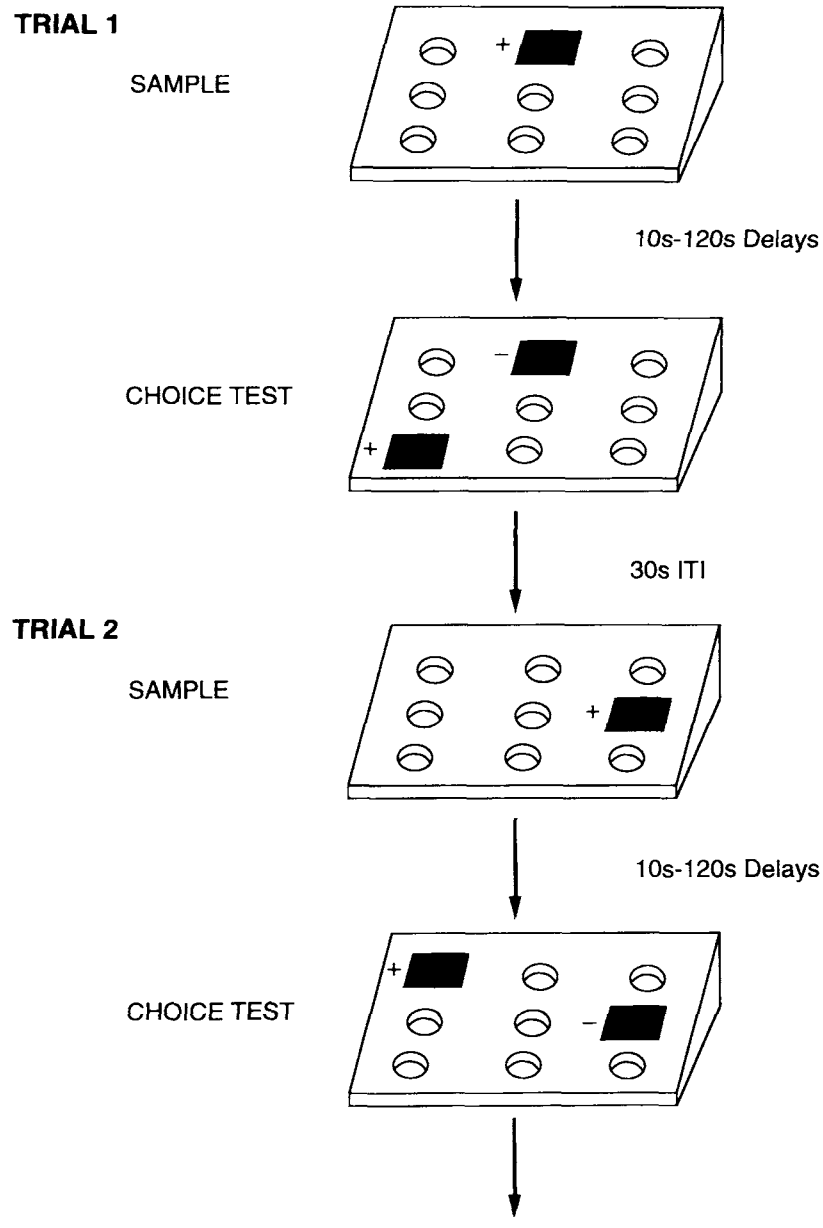

Figure 7. Spatial delayed nonmatching to sample. In the basic task, the monkey is presented with a plaque over one well (sample) and finds the reward (+) after displacing it. Ten seconds later, the monkey is given a choice between the sample well (−) and a new well (+), both covered by identical plaques, and finds a reward only if it displaces the plaque covering the new location on the tray. New pairs of wells are used in successive trials, which are separated by 30-s intervals. On the performance test, delay intervals between sample presentation and choice are increased successively from 10 to 30, 60, and 120 s for 100 trials each.

plaque, and the monkey was allowed to displace it and retrieve the food reward. Ten seconds later, the monkey was presented with a choice test in which the covered sample well, now unbaited, was paired with a second covered, and baited, well. After the monkey made a choice, there was a 30-s intertrial interval, following which a new trial was presented in the same way, using two new locations on the test tray. Twenty trials were presented daily, according to one of six sequences of 20 pairs that had been pseudorandomly selected from a list of all possible pairings. Within each sequence, near–far and left–right positions of the sample vis-à-vis the paired location were counterbalanced pseudorandomly. Monkeys were trained until they reached the criterion of 90 correct choices in 100 trials distributed over 5 consecutive days. Monkeys that could not attain the criterion within 1,000 trials were allowed up to 500 additional trials with double presentation of the sample location. The two presentations of the sample were separated by a 10-s interval, with the baiting pseudorandomly counterbalanced. When the monkeys had reached criterion or the limit of testing, they were given a performance test in which the delays between the sample and the choice test increased from 10 s to 30, 60, and 120 s. At each delay, the monkeys were tested for 100 trials (20 trials per session for 5 consecutive days). Monkeys requiring double sample presentation during the learning phase continued to receive double sample presentations during the performance test.

Results and Discussion

Tactile DNMS

The number of trials and errors each monkey required to learn the tactile DNMS in complete darkness and the scores they obtained at each delay of the performance test are presented in Table 4. The normal monkeys and monkeys with area TE lesions met the criterion of learning in an average of 357 and 510 trials, respectively. By contrast, none of the monkeys with early medial temporal lesions achieved criterion within 1,000 trials, and the training of 2 of the 3 that failed to achieve 75% correct responses was discontinued. The three remaining monkeys received the correction training, 2 achieving criterion and the 3rd attaining 85% correct in the last 100 trials. Because none of the monkeys in Group AH succeeded without correction training, group differences were analyzed by a nonparametric Kruskal-Wallis one-way analysis of variance. This yielded a significant effect of lesion for both trials, $H(2) = 11.13, p < .004$, and errors, $H(2) = 10.40, p < .006$, to criterion. Paired comparisons indicated that Group AH differed significantly from Groups N and TE (all $ps < .02$), which did not differ from each other (Figure 8, left panel).

The scores on the subsequent performance test are shown in Figure 8 (right panel). A Lesion × Condition analysis of variance with repeated measures revealed significant main effects, $F(2, 10) = 12.65, p < .002$, and F(Greenhouse-Geisser 2, 18) = 10.90, $p < .001$, respectively, but no interaction. Paired comparisons (Tukey) indicated that Group AH performed significantly worse than both Group N ($p < .001$) and Group TE ($p < .03$) which, again, did not differ from each other. In addition, in all groups, scores decreased significantly with increasing delays.

Table 4
Tactile Delayed Nonmatching to Sample; Learning and Performance

		Acquisition			Correction			Delay			
Group/case	Sex	T	E	%	T	E	%	30 s	60 s	120 s	AVG
N											
N-2	F	440	105	92	—	—	—	92	94	78	88
N-3	F	380	140	91	—	—	—	86	79	76	80
N-6	F	500	108	92	—	—	—	87	83	73	81
N-8	M	440	93	90	—	—	—	80	79	72	77
N-11	M	180	41	90	—	—	—	90	84	96	90
N-14	M	200	42	90	—	—	—	90	93	83	89
M		357	88	91				88	85	80	84
TE											
TE-1	F	540	116	91	—	—	—	88	83	82	84
TE-8	F	260	64	90	—	—	—	79	85	72	79
TE-4	M	560	157	90	—	—	—	84	75	72	77
TE-7	M	680	198	90	—	—	—	69	77	74	73
M		510	134	91				80	80	75	78
AH											
AH-1	F	1000[a]	418	58	—	—	—	—	—	—	—
AH-3	F	1000[a]	210	85	460	49	92	80	65	60	68
AH-2	M	1000[a]	279	73	—	—	—	—	—	—	—
AH-4	M	1000[a]	265	83	100	24	90	72	62	61	65
AH-7	M	1000[a]	396	68	500	118	85	78	64	66	69
M		1000	314	73	353	64	89	77	64	62	67

Note. Scores are number of trials, T, and total number of errors, E, preceding criterion in acquisition and in correction training and percentage of correct responses in 100 trials at each delay interval; % indicates percentage of correct responses during criterion (last 100 trials). AVG denotes average across the three delays. Group N = normal controls, Group TE = monkeys with neonatal inferior temporal lesions, Group AH = monkeys with neonatal medial temporal lesions, F = female, M = male.
[a]Failure to reach criterion within the limit of testing.

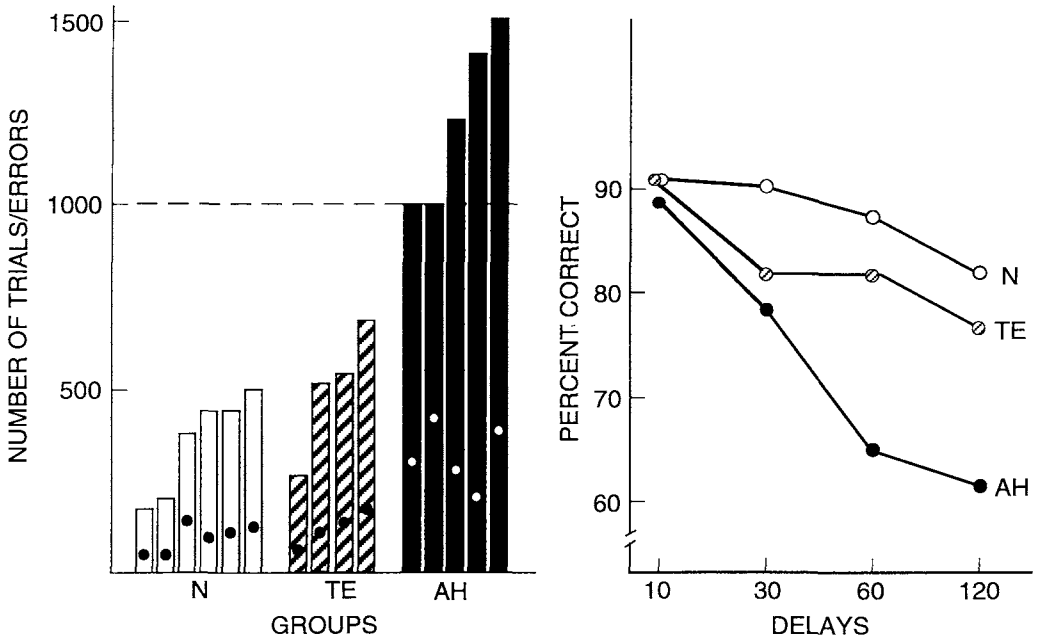

Figure 8. Left panel: Trials (bars) and errors (circles) to criterion in tactile delayed nonmatching to sample. Each bar represents one monkey. Scores over 1,000 trials represent correction training. Right panel: Average scores across delays. The first point of the curve indicates the average final score achieved during the last 100 trials of learning, which entailed recognizing a single object after 10 s. Animals were tested on the three remaining conditions of gradually increasing delays for 100 trials each. Group N = normal controls, Group TE = monkeys with neonatal inferior temporal lesions, and Group AH = monkeys with neonatal medial temporal lesions.

Tactile discrimination

The number of trials and errors to criterion did not differ significantly for the two pairs of objects in any of the groups, as determined by a nonparametric Friedman one-way analysis of variance. Therefore, the average scores for the two pairs were submitted to a nonparametric Kruskal-Wallis analysis of variance. The effect of lesion was significant, $H(2) = 7.26, p < .03$, and $H(2) = 6.14, p < .05$, for trials and errors, respectively, indicating that, unexpectedly, the monkeys in Group N needed more trials and made more errors (average 60 trials and 18 errors) than the animals in both Group TE (21 trials and 7 errors) and Group AH (25 trials and 7 errors). These differences were confirmed by paired comparison tests: Group TE versus Group N, $U(1) = 12.0, p < .03$, and $U(1) = 12.0, p < .03$, for trials and errors, respectively; Group AH versus Group N, $U(1) = 19.5, p < .02$, and $U(1) = 18.5, p < .04$, for trials and errors, respectively. (Because of this unexpected finding, we examined the data for each discrimination separately; in the first discrimination, though not in the second, each of the 3 monkeys with TE lesions required more trials and errors than all but 1 of the 5 with AH lesions, but these differences fell short of significance.)

Spatial DNMS

Results on the spatial DNMS are shown in Table 5 and Figure 9. Groups N and TE learned the task in an average of 293 and 353 trials, respectively, whereas, again, none of the animals in Group AH reached criterion within the limit of testing. Three of the 5 monkeys of Group AH who failed to learn the task in 1,000 trials (AH-3, AH-4, and AH-7) were given the correction training with double presentation of the sample. Following this correction procedure, 1 monkey (AH-4) reached the criterion after 100 additional trials, whereas the 2 others (AH-3 and AH-7) obtained 86% and 87%, respectively, in the last 100 trials. A nonparametric analysis (Kruskal-Wallis) revealed a significant effect of lesion for both trials and errors, $H(2) = 9.67, p < .008$, and $H(2) = 9.64, p < .008$, respectively. Paired comparisons (Mann-Whitney) indicated that Group AH required significantly more trials and made more errors than both Groups N, $U(1) = 0, p < .004$, and $U(1) = 0, p < .006$, respectively, and TE, $U(1) = 0, p < .01$, and $U(1) = 0, p < .05$, respectively, which did not differ from each other.

Further evidence of a spatial memory deficit in the animals with neonatal medial temporal lesions was provided by the performance test (Table 5 and Figure 9, right panel). A Lesion × Condition analysis of variance with repeated measures revealed significant main effects of lesion and condition, $F(2, 9) = 27.81, p < .001$, and F(Greenhouse-Geisser 1, 12) = $14.15, p < .002$, respectively, but not for their interaction. Paired comparisons (Tukey) indicated that Group AH performed significantly more poorly on each of the delays than both Groups N and TE (both $ps < .01$), which did not differ from each other.

Table 5
Spatial Delayed Nonmatching to Sample; Learning and Performance

		Acquisition			Correction			Delay			
Group/case	Sex	T	E	%	T	E	%	30 s	60 s	120 s	AVG
N											
N-2	F	180	33	92	—	—	—	81	85	83	83
N-3	F	540	143	90	—	—	—	90	76	71	79
N-6	F	200	60	91	—	—	—	81	76	68	75
N-8	M	200	48	92	—	—	—	83	85	81	83
N-11	M	240	60	90	—	—	—	80	83	81	81
N-14	M	400	87	92	—	—	—	84	77	71	77
M		293	72	91				83	80	76	80
TE											
TE-1	F	660	143	90	—	—	—	87	83	69	80
TE-4	M	200	61	91	—	—	—	85	74	68	76
TE-7	M	200	61	93	—	—	—	78	72	75	75
M		353	88	91				83	76	71	77
AH											
AH-1	F	1000[a]	292	82	—	—	—	—	—	—	—
AH-3	F	1000[a]	293	83	500	106	86	70	68	62	67
AH-2	M	1000[a]	467	58	—	—	—	—	—	—	—
AH-4	M	1000[a]	232	83	100	9	91	79	63	53	65
AH-7	M	1000[a]	368	65	500	122	87	69	64	61	65
M		1000	330	74	367	79	88	73	65	59	66

Note. Scores are number of trials, T, and errors, E, preceding criterion in acquisition and in correction training and percentage of correct responses in 100 trials at each delay interval; % indicates percentage of correct responses during criterion (last 100 trials). AVG denotes average performance across the three delays. Group N = normal controls, Group TE = monkeys with neonatal inferior temporal lesions, Group AH = monkeys with neonatal medial temporal lesions, F = female, M = male.
[a]Failure to reach criterion within the limit of testing.

Comment

In summary, the animals with neonatal medial temporal lesions had difficulty learning the basic DNMS rule in both the tactile and spatial tests. Further, the possibility that their difficulty in tactile DNMS was due to a tactile discrimination impairment was ruled out. A likely explanation for the slower discrimination learning of the normal as compared with the operated animals is that the former continued longer than the others in attempting to apply the DNMS rule. (The monkeys with early TE lesions showed a tendency in this direction on the first discrimination.) In contrast to the neonatal medial temporal removals, the neonatal inferior temporal lesions had no effect on either tactile or spatial DNMS.

General Discussion

The results of Experiment 1 demonstrate that neonatal damage to medial temporal-lobe structures left visual habit formation intact but severely impaired visual memory formation whether the monkeys were tested in infancy (Bachevalier et al., 1990; Bachevalier & Mishkin, 1994) or in adulthood. Conversely, neonatal damage to inferior temporal cortical area TE yielded significant sparing of both visual habit and visual memory ability (Experiment 1) whether the monkeys were tested in infancy (Bachevalier et al., 1990; Bachevalier & Mishkin, 1994) or in adulthood. Furthermore, as shown in Experiment 2, the loss of visual recognition memory following early medial temporal lesions was accompanied by a severe loss of tactile and spatial memory formation, whereas neonatal lesions of area TE affected neither. Thus, neonatal medial temporal lesions, like those sustained in adulthood, yielded an enduring and global amnesia. By contrast, unlike late area TE lesions, early lesions of this visual area yielded only a mild impairment in both visual learning and memory, indicating significant sparing of these functions when the damage occurs neonatally.

Permanent Global Amnesia After Neonatal Medial Temporal Lesions

The visual memory impairment of the monkeys with neonatal medial temporal lesions was reflected both in their difficulty in relearning the DNMS rule that had been acquired several years earlier and by a sharp decline in their performance when they were tested with long delays and lists. Unlike the unoperated monkeys, which relearned the DNMS rule in adulthood faster than naive normal adult monkeys (24 vs. 105 trials, respectively; the latter scores from Meunier, Bachevalier, & Mishkin, 1993), the neonatally operated monkeys needed about as many trials to relearn the DNMS rule as they had taken to learn it originally as infants (433 vs. 580 trials, respectively). Moreover, the magnitude of the visual recognition loss on the performance test was the same in adulthood as in infancy (drops of 21% vs. 20%, respectively, from the levels of the normal controls). As indicated in Figure 6, this loss was not as large in percentage terms as that found in monkeys that

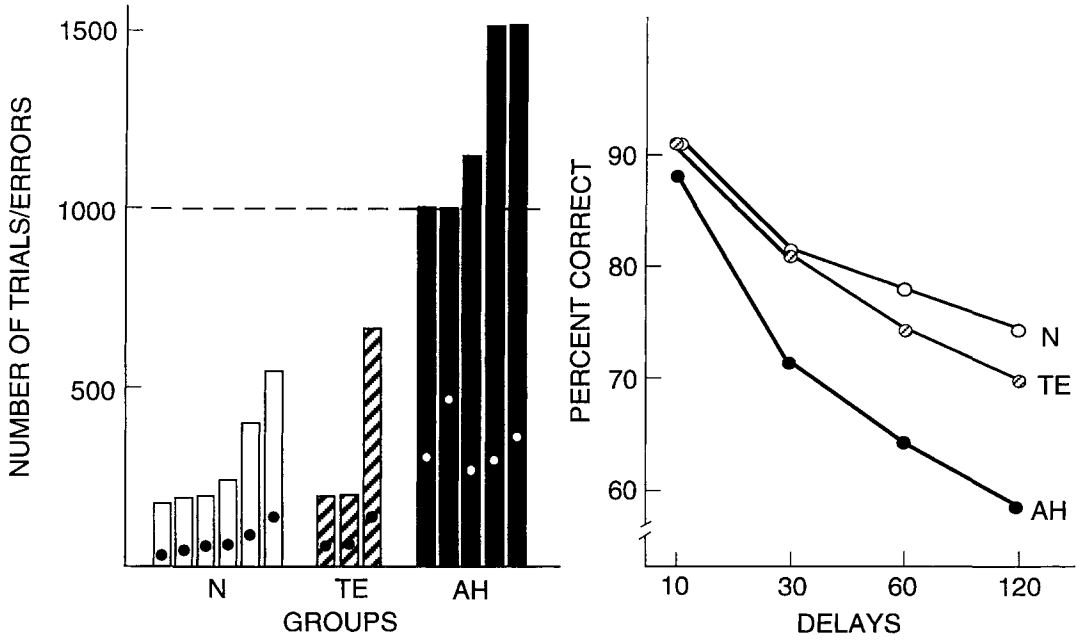

Figure 9. Left panel: Trials (bars) and errors (circles) to criterion in spatial delayed nonmatching to sample. Each bar represents one monkey. Scores over 1,000 trials represent correction training. Right panel: Average scores across delays. The first point of the curve indicates the average final score achieved during the last 100 trials of learning, which entailed recognizing single locations on the test tray after 10 s. Animals were tested on the three remaining conditions of gradually increasing delays for 100 trials each. Group N = normal controls, Group TE = monkeys with neonatal inferior temporal lesions, and Group AH = monkeys with neonatal medial temporal lesions.

had received the same medial temporal removals in adulthood (a drop of 37% from the normal control level; Mishkin, 1978), but the difference did not attain significance.

In tactile DNMS, likewise, the adult monkeys with neonatal medial temporal lesions had extreme difficulty learning the basic rule, with only 3 out of 5 animals attaining criterion and then only after additional training with correction trials. Interestingly, on the performance test, the magnitude of the tactile recognition loss (a drop of 17% from the normal control scores) was equivalent to that of the visual recognition loss (21%), although it was numerically less than the tactile recognition loss found in monkeys that had received medial temporal lesions in adulthood (a drop of 28% from preoperative performance; Murray & Mishkin, 1984). This impairment in tactile DNMS was not clearly attributable to a difficulty in discriminating objects by touch, as indicated by their unimpaired learning of standard tactile discriminations.

Finally, monkeys with early medial temporal lesions performed at least as poorly on spatial as on visual and tactile DNMS. Only 1 of the 5 monkeys attained the 90% criterion and the 2 others that were continued achieved only 86%, all after correction training. They also showed a decline in performance with increasing delays. Loss of memory for spatial locations was previously reported in adult monkeys that had received neonatal damage limited to the hippocampal formation and parahippocampal gyrus (Mahut & Moss, 1986).

Recent studies have demonstrated that the medial temporal lobe tissue that is critical for visual recognition memory is the cortex located in and around the rhinal sulcus. Thus, severe visual recognition deficits were found after combined damage to the entorhinal and perirhinal cortex (Meunier et al., 1993) but not after combined excitotoxic lesions of the amygdala and hippocampus that spared the underlying rhinal and parahippocampal cortex (O'Boyle, Murray, & Mishkin, 1993). Also, severe deficits in tactile as well as visual recognition were found after bilateral damage restricted to the perirhinal and parahippocampal cortex (Suzuki, Zola-Morgan, Squire, & Amaral, 1993). It is thus likely that the enduring loss of visual and tactile recognition memory sustained by the animals with early medial temporal lesions in the present study is attributable mainly to damage to the cortex in and around the rhinal sulcus and not to that of the limbic structures themselves. This proposal is strengthened by recent findings indicating that neonatal ablations of the hippocampal formation that included much of the parahippocampal gyrus but did not encroach on the perirhinal or entorhinal areas appeared to leave visual recognition memory completely intact (Beauregard & Bachevalier, 1993). The proposal regarding the locus of the critical tissue for recognition memory may not extend to spatial memory, in view of the evidence that severe impairment in the latter function can be produced by hippocampal ablations that largely spare the rhinal cortex (Angeli et al., 1993; Parkinson et al., 1988).

Although neonatal medial temporal lesions yielded a severe impairment in both visual and tactile object recognition, there was nevertheless a substantial reduction in the absolute

magnitude of this impairment compared with that following the same lesions in adults. As already indicated, the difference was not significant, and yet the size of the difference, a 21% versus 37% loss in the two operated groups, compared with their normal controls, seems too large to ignore completely, given the small *N*s involved. This difference in degree of deficit was first observed in the earlier study (Bachevalier & Mishkin, 1994), when the present animals were 10 months of age, and two possible explanations for it were advanced at that time. First, the performance of the normal controls tested at 10 months of age did not reach the level attained by the normal controls tested only as adults, and so it seemed possible that with further maturation, the normal infant monkeys, but not those given early medial temporal lesions, might improve their performance and thereby yield a more severe impairment in the operated group as both groups aged. Alternatively, the relative sparing of visual recognition in the early operated group might have been only transitory, such that, with further maturation, their performance might deteriorate and in this way reveal a more severe impairment. The results of the present experiment, however, rule out both possibilities, inasmuch as the performance of neither group, normal or operated, changed appreciably with maturation. The most likely explanation for the seemingly smaller deficit after early than after late lesions now seems to be related to the evidence, reviewed above, that the medial temporal tissue critical for recognition memory is neither the amygdala nor the hippocampus, both of which were totally removed in monkeys with both the early and the late medial temporal lesions, but the cortex located in and around the rhinal sulcus, which was damaged only partially in both. Partial sparing of this tissue could have more beneficial consequences during the period of development than after because the spared cortical tissue may have the connectional plasticity during early development to compensate in part for the damaged cortical tissue (see below). At the same time, the recovery from early medial temporal damage did not attain statistical significance, unlike the recovery from early damage to the inferior temporal cortex.

Permanent, Substantial Sparing of Function Following Neonatal Area TE Lesions

Neonatal removals of area TE, unlike the same removals in adult animals, yielded only a modest impairment in both visual recognition memory and visual habit formation, and a degree of functional sparing was still present when the animals reached adulthood (Figures 3 and 6). The results indicate that compensatory mechanisms operating in infancy have permanent effects. In the case of the early TE lesions, the presumption is that other areas in the occipitotemporal pathway assume the functions of the damaged area, and, indeed, a beginning has been made in the elucidation of the neuroanatomical mechanisms whereby this form of substitution might be achieved. Specifically, in monkeys with neonatal removals of area TE, the anatomical projections of area TEO have been found to undergo two types of reorganization (Webster et al., 1991a, 1991b). First, exuberant projections from area TEO to the lateral basal nucleus of the amygdala and the parahippocampal gyrus—that is, projections that are present in infant monkeys but then retract during normal development—are maintained in the absence of the competing projections from area TE. Second, the normally limited projections from area TEO to the dorsal tip of the lateral nucleus of the amygdala expand to innervate a large portion of the zone no longer occupied by terminals from area TE. Although the particular projections just described are probably not responsible for the permanent sparing of visual learning and memory demonstrated here, inasmuch as neither the amygdala nor the parahippocampal gyrus appears to be critical for either visual recognition or habit formation, it has been found in combined-lesion studies that area TEO and other occipitotemporal areas outside TE do participate in this functional sparing (Webster et al., 1994, 1995). On the basis of these behavioral and neuroanatomical findings, it seems likely that the maintenance of exuberant projections and the sprouting of new ones from visual areas outside TE to structures that are critical for visual recognition and habit formation mediate the functions that would otherwise fail after neonatal loss of the projections from area TE. These compensatory projections, however, remain to be identified.

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