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Effects of Selective Neonatal Temporal Lobe Lesions on Socioemotional Behavior in Infant Rhesus Monkeys (*Macaca mulatta*)

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Normal infant monkeys and infant monkeys with neonatal damage to either the medial temporal lobe or the inferior temporal visual area were assessed in dyadic social interactions at 2 and 6 months of age. Unlike the normal infant monkeys, which developed strong affiliative bonds and little or no behavioral disturbances, the lesioned monkeys (each of which was observed with an unoperated control) exhibited socioemotional abnormalities and aberrant behaviors. The socioemotional changes predominated at 6 months of age and were particularly severe in monkeys with medial temporal lesions. In both the pattern and time course, the socioemotional deficits produced by the neonatal medial temporal lesions bear a striking resemblance to the behavioral syndrome in children with autism. Further analysis of these lesion-induced abnormalities in nonhuman primates may therefore provide insight into this debilitating human developmental disorder.

In earlier reports, we presented evidence that ablation of the medial temporal lobe in neonatal monkeys results in a chronic, global memory disorder nearly as severe as that produced by the same lesions in adult monkeys (Bachevalier, Brickson, Hagger, & Mishkin, 1990; Bachevalier & Mishkin, 1994; Málková, Mishkin, & Bachevalier, 1995). This evidence stood in sharp contrast to a marked sparing of visual learning and memory ability that was observed in the above studies after neonatal (as compared with later) removal of the inferior temporal visual area. This pattern of findings indicated that whether or not the plasticity of the immature brain will result in compensatory reorganization of function after early injury depends on the locus of that injury. The question examined in the present study is whether other behavioral and cognitive abilities known to be dependent on the temporal lobe in adult monkeys are also differentially affected by early selective damage to this region.

Bilateral ablation of the temporal lobes in adult monkeys produces a complex set of symptoms known as the Klüver–Bucy syndrome (Klüver & Bucy, 1938, 1939). This syndrome includes visual agnosia, loss of fear, hypoemotionality, hypersexuality, increased oral tendency, and loss of social interactions. Further investigation in adult monkeys revealed that most of these behavioral changes can occur after either aspiration or selective neurotoxic lesions of the amygdala (for reviews, see Kling & Brothers, 1992; Meunier, Bachevalier, Murray, Málková, & Mishkin, 1999), after ablations of the anterolateral temporal neocortex (Akert, Gruesen, Woolsey, & Meyer, 1961; Franzen & Myers, 1973; Horel, Keating, & Misantone, 1975; Horel & Misantone, 1974; Iwai, Nishio, & Yamaguchi, 1986; Meyer, 1972; Myers & Swett, 1970; Raleigh & Steklis, 1981), or after disconnection of fibers coursing between these two regions (Horel & Misantone, 1974). As yet, there has been little investigation to determine whether similar behavioral changes will result from selective temporal lobe damage incurred in early infancy. Thompson and his colleagues (Thompson, 1969; Thompson, Schwartzbaum, & Harlow, 1969; Thompson & Towfighi, 1981) reported that aspiration lesions of the amygdala in 2-month-old monkeys yield changes in social behavior that are similar in many ways to those described after identical lesions in adult monkeys. However, the socioemotional effects of more extensive early medial temporal lesions or of early temporal neocortical removals have not been examined before. In the present study, we investigated the socioemotional behavior of the infant monkeys with selective neonatal temporal lobe lesions that had participated in our learning and memory studies. Preliminary reports of the present investigation have appeared elsewhere (Bachevalier, 1991, 1994; Bachevalier & Merjanian, 1994).

METHOD

Subjects

The infant subjects were 24 full-term rhesus monkeys (*Macaca mulatta*) of both sexes, weighing between 417 and 734 g. Twelve of these monkeys were born at the National Institutes of Health (NIH) Animal Center (Poolesville, MD) of imported mothers bred at the Perrine, FL, colony, and the others were born of mothers bred at the NIH Veterinary Resources Branch (Bethesda, MD). Immediately after birth, the infants were brought to a primate nursery in the Laboratory of Neuropsychology, where they were assigned to dyads or triads that were reared together part time. Two

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dyads each consisted of 1 unoperated control monkey and 1 that was to receive a bilateral lesion of the medial temporal lobe, referred to here as an *AH lesion* (amygdalo–hippocampectomy) for ease of comparison with other reports on the same animals. Another dyad consisted of 1 unoperated control monkey and 1 that was to receive a bilateral lesion of the inferior temporal cortex, referred to here as a *TE lesion* (ablation of Brodmann's Area TE), again for ready comparison with other reports on these same animals. Four triads each consisted of 1 unoperated control monkey, a 2nd that was to receive an AH lesion, and a 3rd that was to receive a TE lesion. Finally, two triads each consisted of 3 unoperated control monkeys, formed to assess normal social behavior under our experimental conditions. Thus, there were 6 infant monkeys (3 male and 3 female) with neonatal AH lesions, 5 infant monkeys (2 male and 3 female) with neonatal TE lesions, 7 infant unoperated control monkeys (4 male and 3 female), and 6 normal infant monkeys (4 male and 2 female). For clarity, these groups are referred to as follows: AH, TE, C with AH, and C with TE (for unoperated control monkeys paired during recording of socioemotional behavior with AH and TE monkeys, respectively) and N (for normal monkeys paired with other normal monkeys). All observations were carried out on dyads consisting of the following: AH+C, TE+C, and N+N.

All of the infant monkeys were fed a diet of infant Similac formula (SMA with iron) and, at 3 weeks of age, when the infant monkeys were self-feeding, their diet was supplemented with banana pellets (190 mg, P.J. Noyes, Cleveland, OH). At the age of 3 months, the milk ration was supplemented with Purina monkey chow and Vidaylin multivitamin plus iron tablets (Ross Laboratory, Columbus, OH), and fresh fruit were given once a week. Water was always available.

Rearing Experience

On arrival in the primate nursery, all newborn monkeys were placed in large-mesh cages under open radiant incubators, each of which accommodated two cages and thus allowed visual, auditory, and some somatosensory contact between a pair of monkeys. Contact comfort was provided by a cotton towel hung from the top of the cage and several towels placed on the floor. At 2 months of age, the monkeys were transferred to larger wire cages and housed individually. From the time of their arrival in the primate nursery until they were 1.5 years of age, they were handled by the experimenters and caretakers several times daily. Also, they were given daily sessions of 4 to 6 hr each during which the monkeys of a given dyad or triad were placed together in an enclosure (either a playpen for the infants up to 8 months of age or a large cage for monkeys from 8 to 16 months of age) located in the nursery; the enclosures were equipped with toys and towels.

Surgery

Surgery was performed aseptically by aspiration in two unilateral stages: the lesion on the left when the monkeys were about 1 week of age and the one on the right when they were about 3 weeks of age. The monkey was anesthetized with a 1:10 mixture of acepromazine and ketamine (15 mg/kg, im) supplemented throughout surgery as needed. A complete description of the surgical procedures, pre- and postoperative care, and recovery of these monkeys is available elsewhere (Bachevalier et al., 1990).

The medial temporal or AH lesion was intended to be identical to those made previously in adult monkeys (e.g., Murray & Mishkin, 1984). This removal included the amygdaloid complex, hippocampal formation, and the periamygdaloid, entorhinal, and parahippocampal cortices. The rostral part of the lesion was made through an orbitofrontal approach. After this tissue was elevated slightly to permit visualization of the rostral face of the medial temporal lobe, the entire amygdaloid complex was removed, as well as the periamygdaloid cortex and the rostral portion of the entorhinal cortex (Area 28), including the medial bank of the rhinal sulcus. The caudal part of the lesion was made through a supralabyrinthine approach. After the cortex was elevated at the occipitotemporal junction to permit visualization of the ventrocaudal portion of the temporal lobe, the entire hippocampus was removed, as well as the subjacent parahippocampal cortex lying medial to the fundus of the occipitotemporal sulcus and the posterior portion of the entorhinal cortex, including the medial bank of the rhinal sulcus.

The inferior temporal or TE lesions were also intended to be identical to those made earlier in adult monkeys (Phillips, Malamut, Bachevalier, & Mishkin, 1988). These removals extended dorsoventrally from the fundus of the superior temporal sulcus (STS) to the fundus of the occipitotemporal sulcus and to the lateral lip of the rhinal sulcus, and rostrocaudally from the anterior tip of STS to a line 9 mm in front of and parallel to the ascending limb of the inferior occipital sulcus.

When the removals were completed, the wounds were sutured in anatomical layers, and the monkey was placed in an incubator until it recovered from anesthesia. After each surgery, the monkey received acetaminophen (Tylenol, 10mg/kg orally) for postoperative analgesia, an antibiotic (chloramphenicol; 12mg/kg orally) as a prophylactic measure, and dexamethasone phosphate (0.5mg/kg im) to counteract brain edema.

Lesion Assessment

The extent of the lesions was evaluated histologically in all but 2 monkeys (AH-4 and TE-7), in which it was evaluated with magnetic resonance imaging (Saunders, Aigner, & Frank, 1990) when these monkeys were about 7 years of age. Detailed descriptions of the lesions have already been reported (Bachevalier et al., 1990; Bachevalier & Mishkin, 1994). Schematic illustration of a representative lesion of each type, Cases AH-6 and TE-8, are presented in Figure 1.

All medial temporal lobe removals were complete, except for bilateral sparing of the most caudal 1–2 mm of the hippocampus in three cases (AH-5, AH-6, and AH-7). However, all lesions included the fundus as well as the medial bank of the rhinal sulcus along its entire length, thus encroaching on perirhinal Area 35 in addition to removing entorhinal Area 28. Also, all monkeys sustained a small amount of unintended damage to the ventrolateral portion of inferior temporal area TEO, unilaterally in cases AH-3, AH-6, and AH-7, and bilaterally in cases AH-4, AH-5, and AH-8. This damage, which presumably resulted from mechanical or ischemic injury during surgery, was judged to be substantial (i.e., about 10% of TEO) only in AH-8, in which it also extended caudally to include a portion of the ventromedial occipital cortex (see Bachevalier & Mishkin, 1994, Figure 5).

Removals of Area TE were largely as intended. In three of the cases (TE-6, TE-7, and TE-8), the ventromedial border of the lesion spared a strip of tissue about 1–2 mm wide lateral to the lateral lip of the rhinal sulcus bilaterally, thereby sparing most of perirhinal Area 36. In one case (TE-5), only the rostral third of this perirhinal tissue was spared bilaterally. A small amount of unintended damage was found in the most anterior portion of Area TEO (the cortical division caudal to Area TE), unilaterally in Case TE-5 and bilaterally in Case TE-8 (see Figure 1, levels +5 and 0).

Behavioral Assessment

The monkeys were assessed for socioemotional behavior when they were approximately 2 months old (range = 1.6–3.1 months) and again when they were about 6 months old (range = 4.5–7.3 months). During the course of the socioemotional investigation described here, none of the monkeys were tested concurrently on any cognitive tasks. Such testing had been performed before they were 2 months of age (visual paired comparison: Bachevalier, Brickson, & Hagger, 1993), again when they were between 3 months and 6 months of age (visual discrimination habit formation: Bachevalier et al., 1990), and then after they were 10 months of age (visual, tactile, and spatial recognition: Bachevalier & Mishkin, 1994; Málková et al., 1995).

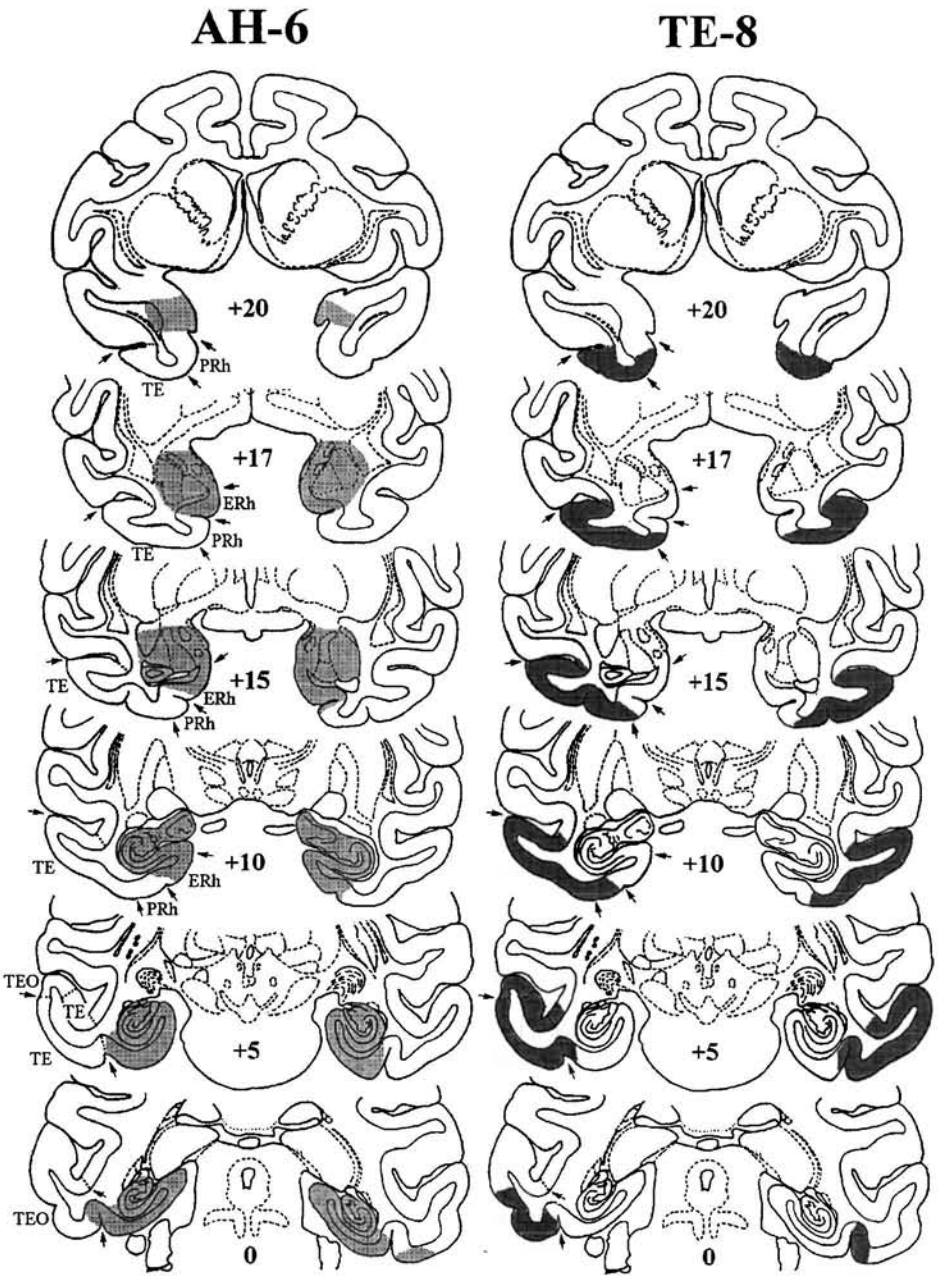

Figure 1. Coronal sections through the extent of damage in two representative cases, one with a neonatal medial temporal lesion (AH-6; light shading) and the other with a neonatal inferior temporal lesion (TE-8; dark shading). Delineation of the entorhinal and perirhinal cortical fields follows the description of Meunier, Bachevalier, Mishkin, and Murray (1993). Arrows point to cytoarchitectonic borders. ERh = entorhinal cortex; PRh = perirhinal cortex; TE = inferior temporal cortical Area TE; TEO = inferior temporal cortical Area TEO.

For socioemotional assessment, the monkeys were placed in a wire cage (50 cm wide, 100 cm long, and 50 cm high) containing several towels and toys. The cage was placed on a table, 85 cm high, located in the center of the infant nursery. For each daily session, which occurred between 11:00 a.m. and 1:00 p.m., 2 infant monkeys that formed an infant monkey dyad, either AH+C, TE+C, or N+N, were transferred from their living cages to the testing cage. The daily session consisted of a 3-min adaptation period followed by two 5-min periods during which the monkeys' behavior was videotaped; these two recording periods were separated by a 5-min period without recording. At the end of the 18-min session, the 2 monkeys were replaced in their individual living cages. This procedure was repeated for 6 consecutive days both when the monkeys were 2 months old and again when they were 6 months old.

Behavioral Scoring

The videotaped behaviors were classified into 11 different behavioral categories plus the category *not identified* (see Table 1). These categories were thus exhaustive but not mutually exclusive (e.g., manipulation and locomotion could co-occur). The frequency and duration of the categorized

Table 1
Behavioral Categories

Behavior	Interobserver reliability: Frequency	Interobserver reliability: Duration	Description
General activity			
Passive behavior	.94	.83	Inactive or asleep
Manipulation	.89	.96	Handles, chews, licks, or mouths
Locomotion	.93	.94	Walks, runs, climbs, or jumps
Social behavior			
Approach	.79	.88	Initiates social contact, that is, moves toward, grooms, clings to, chases, plays, follows, or plays with the other, or engages in sexual activity with the other
Accepts approach	.75	.58	Accepts or reciprocates social contact (see above) initiated by the other
Active withdrawal	.63	.65	Moves away or makes an avoidance response after other attempts to initiate social contact (see above)
Dominant approach	.93	.82	Makes threatening gestures, takes toy away from other, or otherwise interferes with other; rejects approach by pushing other away; or engages in any active antisocial behavior
Eye contact	.96	.97	Looks toward the eyes or face of the other monkey
Disturbances of behavior			
Self-directed behaviors	.75	.95	Engages in self-directed behaviors other than sucking (see above), that is, self-grooms, hugs head, self-grabs and bites, presses face with hands, self-holds, closes fists, self-clutches, sexually self-stimulates, lays prone, or puts head on chest
Locomotor stereotypies	.85	.81	Swings from top of cage, somersaults, circles
Temper tantrums	.86	.99	Makes high-pitched vocalizations accompanied with jerky movements
Not identified		.97	Behavior not determined with confidence

Note. Interobserver reliability was calculated by Pearson's rank coefficient correlation.

behaviors were recorded with a Tandy 102 portable computer. The behavioral categories *approach* and *accepts approach* were summed across both members of each dyad to provide a composite score indicating the amount of total social contact per dyad.

Over the course of the study, samples of the videotapes were scored independently by two observers; interobserver reliability across the categories averaged 0.84 for frequency and 0.85 for duration (see Table 1). All of the tapes were subsequently rated by one observer, who was unaware of the nature of a monkey's lesion (AH or TE) but not to the fact that it had received surgery, because its head had been shaved resulting in abnormal regrowth of fur.

Data Analysis

For each behavioral category, each monkey had received two scores: frequency and duration for each 5-min recording period. The scores for each measure were then summed over the 60 min (12 periods) of recording, and these sums were used for group comparisons. The behavioral effects of the two types of lesion were first determined separately. Each of these scores for each category was then subjected to unifactorial analysis of variance (ANOVA) at each age. In each case, one ANOVA compared Groups N, AH, and C (the controls for AH) and another compared Groups N, TE, and C (the controls for TE). Bonferroni adjusted pairwise comparisons were used for all post hoc tests.

To test the effect of age, we used a 3 × 2 (Group × Age) repeated measures ANOVA. For this analysis, two of the AH+C dyads and two of the TE+C dyads at 6 months of age were excluded (see Table 2), because their behavior at 2 months of age could not be assessed accurately owing to technical difficulties with the video recording.

The scores of the two lesion groups (AH and TE) were next compared directly with each other and with those of the normal group (N). For these comparisons, the monkeys' scores on each behavioral category were analyzed by a 3 × 2 (Group × Age) repeated measures ANOVA. For all ANOVAs, p values were calculated using degrees of freedom corrected for repeated measures by the Huynh–Feldt epsilon method (Huynh & Feldt, 1976).

RESULTS

The average frequency scores for each group are shown in Tables 2 and 3, and the average duration scores are shown in Figures 2 and 3. The pattern of behavioral activities recorded in the normal dyads is reported first. Next, the effects of each of the two types of neonatal lesion on each behavioral category are described, and the effects of the two lesions are then compared with each other. Finally, the behavioral pattern found in the unoperated control monkeys paired separately with a neonatally operated monkey of each type (AH and TE) is described.

Behavioral Activity in the Normal Dyads

At 2 months of age, the normal monkeys paired together (Group N) spent most of the time in manipulation (see Figure 2B) and total social contact (see Figure 3C). They displayed virtually no behavior considered to be abnormal, such as active withdrawal, locomotor stereotypies, self-directed behaviors, or temper tantrums. Although the overall pattern of behavioral activities was much the same at 6 months of age as it was at 2 months, statistical comparison between the two ages revealed a decrease in duration of manipulation, $t(11) = 3.65$, $p < .004$; an increase in duration of locomotion, $t(11) = 2.18$, $p = .05$; and a decrease in the frequency of temper tantrums, $t(11) = 2.43$, $p < .03$. Finally, although total social contact did not change with age (see Table 3 and Figure 3C), at age 2 months this category consisted primarily of following or clinging to the other monkey, whereas at age 6 months it was replaced by rough-and-tumble play and chasing. This increase in social play behavior from 2 to 6 months of age was associated with a significant increase in eye contact, $t(11) = 2.71$, $p < .02$, and $t(11) = 2.24$, $p < .05$, for duration and frequency, respectively (see Figure 3D).

Table 2
Means (±SEM) for Frequency of Each Behavioral Category for the 60 Min of Recording

Group	N	C with AH	AH	C with TE	TE
General activity					
Passive behavior					
2 months	27.0 ± 4.1	36.5 ± 11.4	117.5 ± 10.5	61.0 ± 39.6	72.0 ± 9.5
6 months	35.3 ± 6.8	25.5 ± 10.9	36.0 ± 7.9	34.4 ± 16.4	33.8 ± 9.9
6 months[a]		13.3 ± 3.3	40.3 ± 11.0	10.3 ± 5.8	35.7 ± 17.7
Manipulation					
2 months	125.4 ± 18.6	163.5 ± 27.5	90.8 ± 37.6	127.7 ± 32.8	103.0 ± 6.7
6 months	123.0 ± 9.3	114.0 ± 17.8	150.0 ± 18.9	127.0 ± 23.7	135.4 ± 21.7
6 months[a]		88.0 ± 10.9	157.0 ± 26.4	114.0 ± 31.1	141.7 ± 37.2
Locomotion					
2 months	200.5 ± 31.4	290.8 ± 37.2	172.3 ± 50.1	240.3 ± 45.9	268.7 ± 28.6
6 months	220.7 ± 15.4	206.0 ± 26.2	222.7 ± 31.4	178.2 ± 16.4	258.8 ± 20.0
6 months[a]		187.3 ± 29.1	208.0 ± 47.1	182.3 ± 29.4	253.3 ± 34.3
Social behavior					
Approach					
2 months	52.7 ± 13.6	59.8 ± 19.5	36.3 ± 9.8	107.3 ± 45.6	107.7 ± 46.7
6 months	66.5 ± 15.7	38.0 ± 2.5	19.8 ± 7.5	28.8 ± 5.9	37.8 ± 10.6
6 months[a]		38.3 ± 4.0	15.7 ± 10.4	31.3 ± 8.4	36.0 ± 18.9
Accepts approach					
2 months	68.5 ± 19.8	47.5 ± 8.5	113.8 ± 39.7	84.7 ± 33.2	104.0 ± 45.4
6 months	66.2 ± 15.9	14.3 ± 7.0	38.8 ± 7.0	30.8 ± 9.3	22.8 ± 4.1
6 months[a]		12.3 ± 10.9	35.8 ± 10.6	28.3 ± 16.4	22.0 ± 5.3
Eye contact					
2 months	30.8 ± 2.9	49.5 ± 26.4	22.5 ± 7.5	56.3 ± 12.1	62.7 ± 11.3
6 months	46.7 ± 4.9	37.3 ± 8.6	35.7 ± 10.2	45.6 ± 14.9	85.2 ± 15.9
6 months[a]		42.0 ± 11.4	37.5 ± 14.7	66.3 ± 11.7	97.0 ± 20.7
Active withdrawal					
2 months	0.2 ± 0.1	0.0 ± 0.0	1.8 ± 1.4	0.0 ± 0.0	0.0 ± 0.0
6 months	0.4 ± 0.3	0.8 ± 0.4	17.7 ± 6.3	0.8 ± 0.8	12.4 ± 3.3
6 months[a]		0.8 ± 0.5	23.8 ± 7.8	1.3 ± 1.3	17.0 ± 3.0
Dominant approach					
2 months	6.9 ± 2.1	1.3 ± 0.9	0.0 ± 0.0	5.0 ± 2.5	0.3 ± 0.3
6 months	3.7 ± 1.2	17.2 ± 5.7	1.3 ± 0.6	24.4 ± 5.6	9.8 ± 5.5
6 months[a]		17.8 ± 1.2	0.8 ± 0.5	30.7 ± 6.9	4.7 ± 4.2
Disturbances of behavior					
Locomotor stereotypies					
2 months	0.5 ± 0.2	2.7 ± 2.7	1.0 ± 0.7	0.0 ± 0.0	7.3 ± 7.3
6 months	4.3 ± 1.8	4.8 ± 0.5	9.3 ± 5.0	3.2 ± 1.3	12.8 ± 7.9
6 months[a]		5.0 ± 0.4	3.3 ± 1.3	2.0 ± 1.0	15.3 ± 13.8
Self-directed behaviors					
2 months	0.5 ± 0.2	1.0 ± 0.7	1.8 ± 1.2	0.0 ± 0.0	2.0 ± 1.0
6 months	0.7 ± 0.3	9.3 ± 6.3	27.3 ± 7.3	7.0 ± 4.1	7.0 ± 3.7
6 months[a]		11.0 ± 9.7	21.8 ± 11.7	3.0 ± 1.5	10.3 ± 4.3
Temper tantrums					
2 months	3.8 ± 1.5	8.5 ± 4.7	18.8 ± 3.8	0.0 ± 0.0	4.3 ± 2.3
6 months	0.3 ± 0.3	12.2 ± 11.9	1.3 ± 1.3	4.6 ± 2.9	0.4 ± 0.2
6 months[a]		18.0 ± 18.0	2.0 ± 2.0	5.0 ± 5.0	0.6 ± 0.3

Note. N = normal monkeys paired with other normal monkeys; C with AH = unoperated control monkeys paired with monkeys with neonatal medial temporal lobe lesions (AH); C with TE = unoperated control monkeys paired with monkeys with neonatal inferior temporal lesions (TE).
[a] These means are based on 6 animals per group, including the 2 for each group (C with AH, AH, C with TE, and TE) that were not included at 2 months of age (see the Data Analysis section).

Behavioral Activity After Neonatal AH or TE Lesions

General Activity

Passive Behavior

AH lesion. At 2 months of age, monkeys in Group AH showed far more passive behavior than those in either Group N or C (see Table 2 and Figure 2A). This was reflected in a group effect for both duration, $F(2, 17) = 6.70$, $p < .007$ (pairwise comparisons: AH > N, $p = .006$), and frequency, $F(2, 17) = 26.5$, $p < .000$ (pairwise comparisons: AH > N and C, all ps = .001). These differences became negligible at 6 months of age because of a sharp decrease in passive behavior of Group AH. The decrease was reflected in a Group × Age interaction for both duration, $F(2, 17) = 11.18$, $p < .001$, and frequency, $F(2, 17) = 31.28$, $p < .000$.

TE lesion. At 2 months of age, monkeys in both Groups TE and C were more passive than those in Group N. This was reflected in a significant group effect for frequency, $F(2, 15) = 5.29$, $p < .02$ (pairwise comparison, TE > N, $p = .02$). This difference, however, disappeared by the age of 6 months because of a decrease of passive behavior in both Groups TE and C. The decrease was

Table 3
Means (±SEM) for Frequency of Social Contacts Between 2 Monkeys in a Dyad Across the 60 Min of Recording

Group	N + N	AH + C	TE + C
2 months	230.8 ± 75.0	257.3 ± 41.4	403.7 ± 38.7
6 months	265.3 ± 29.3	173.0 ± 111.0	120.2 ± 23.5
6 months[a]		102.0 ± 27.7	117.7 ± 41.2

Note. N + N = dyads including 2 normal monkeys; AH + C = dyads including 1 unoperated control and 1 monkey with an amygdalo–hippocampectomy lesion; TE + C = dyads including 1 unoperated control and 1 monkey with an Area TE lesion.
[a] These means are based on 6 animals per group, including the 2 for each group (C with AH, C with TE, and TE) that were not included at 2 months of age (see the Data Analysis section).

reflected in a Group × Age interaction for duration, $F(2, 15) = 3.65$, $p = .05$, and frequency, $F(2, 15) = 5.48$, $p < .02$.

AH versus TE lesions. Although at 2 months of age, the infant monkeys in both lesion groups showed greater passivity than did normal infants, the monkeys with AH lesions were the most passive of all (AH > TE, $p = .02$). This difference disappeared by 6 months of age, when both lesion groups showed normal amounts of passive behavior.

Manipulation

AH lesion. At 2 months of age, Group AH manipulated objects and parts of the cage less than the monkeys of Groups N and C, as indicated by a group effect for duration, $F(2, 17) = 6.40$, $p < .008$ (pairwise comparison: AH < N, $p = .007$; see Table 2 and Figure 2B). By 6 months of age, however, Groups AH and C displayed more manipulation than Group N, as indicated by a group effect for duration, $F(2, 21) = 4.26$, $p < .03$ (pairwise comparison: C > N, $p = .03$). Thus, whereas manipulation decreased over time in Group N (see normal dyads), it increased in Groups AH and C: Group × Age interaction for both duration, $F(2, 17) = 15.74$, $p < .000$, and frequency, $F(2, 17) = 4.13$, $p < .04$.

TE lesion. At 2 months of age, monkeys in Groups TE and C manipulated objects and parts of the cage less than the monkeys of Group N, as revealed by a group effect for duration, $F(2, 15) = 5.83$, $p < .01$ (pairwise comparison, TE and C < N, all $ps < .05$). At 6 month of age, however, both Groups TE and C displayed more manipulation than monkeys of Group N, as indicated by a group effect for duration, $F(2, 19) = 15.82$, $p < .000$ (pairwise comparisons, TE and C > N, all $ps < .001$). Thus, manipulation increased over time in Groups TE and C: Group × Age, $F(2, 15) = 29.07$, $p < .000$, for duration, just as it had in the AH+C dyads.

AH versus TE lesions. The two types of neonatal lesions yielded similar effects on manipulation; that is, both groups spent less time in this activity at 2 months of age than Group N, and both lesion groups then showed equal increases in this behavior at 6 months of age.

Locomotion

AH lesion. At 2 months of age, the three groups engaged in the same amount of locomotion (see Table 2 and Figure 2C). By contrast, at 6 months, Group N, but not the AH+C dyads, exhibited an increase in locomotion, yielding a Group × Age interaction for frequency, $F(2, 17) = 4.74$, $p < .02$.

TE lesion. At 2 months of age, there were no significant differences among groups. At 6 months, the TE+C dyads, like the AH+C dyads, failed to show the increased locomotion exhibited by Group N, although the Group × Day interaction did not reach significance.

AH versus TE lesions. There were no differences in the effects of the two lesions on locomotion at either age.

Social Behavior

Approach

AH lesion. Although Group AH displayed the least amount of approach, the groups (AH, C, and N) did not differ significantly at either age (see Table 2 and Figure 3A).

TE lesion. Both Groups TE and C engaged in approach somewhat more than Group N at 2 months of age but less than Group N at 6 months, yielding significant Group × Age interactions for both duration, $F(2, 15) = 7.08$, $p < .007$, and frequency, $F(2, 15) = 6.36$, $p < .01$.

AH versus TE lesions. The two lesion groups did not differ significantly at either age, and both lesions groups showed a decrease in this behavior from 2 to 6 months of age.

Accepts Approach

AH lesion. At 2 months of age, Group AH showed accepts approach from their controls more than the normal monkeys in Group N, but this difference did not reach significance (see Table 2 and Figure 3B). By contrast, at 6 months of age, both Groups AH and C showed accepts approach less than monkeys of Group N, as reflected by a group effect for duration, $F(2, 21) = 6.28$, $p < .007$ (pairwise comparisons AH and C < N, all $ps < .02$). Accepts approach remained relatively constant across time in Group N, whereas it decreased markedly in the AH+C dyads: Group × Age interaction for duration, $F(2, 17) = 3.80$, $p < .04$, and for frequency, $F(2, 17) = 4.78$, $p < .02$.

TE lesion. At 2 months of age, there were no significant differences among groups. At 6 months of age, however, both Groups TE and C, like Groups AH and C, showed accepts approach less than Group N, $F(2, 19) = 4.07$, $p < .03$ for duration (pairwise comparisons, TE < N, $p = .08$). Between the two ages, accepts approach did not change in Group N, whereas it decreased substantially in the TE+C dyads: Group × Age interaction, $F(2, 15) = 5.20$, $p < .02$, for frequency.

AH versus TE lesions. At 2 months of age, the two lesion groups showed accepts approach from their unoperated controls about equally (and somewhat above the level of that shown by the monkeys in Group N), whereas at 6 months of age, accepts approach tended to decrease almost equally in the two operated groups (unlike in Group N).

Total Social Contact

AH lesion. At 2 months of age, total social contact was only slightly reduced in the AH+C dyads as compared with the N+N dyads (see Table 3 and Figure 3C). At 6 months, however, this

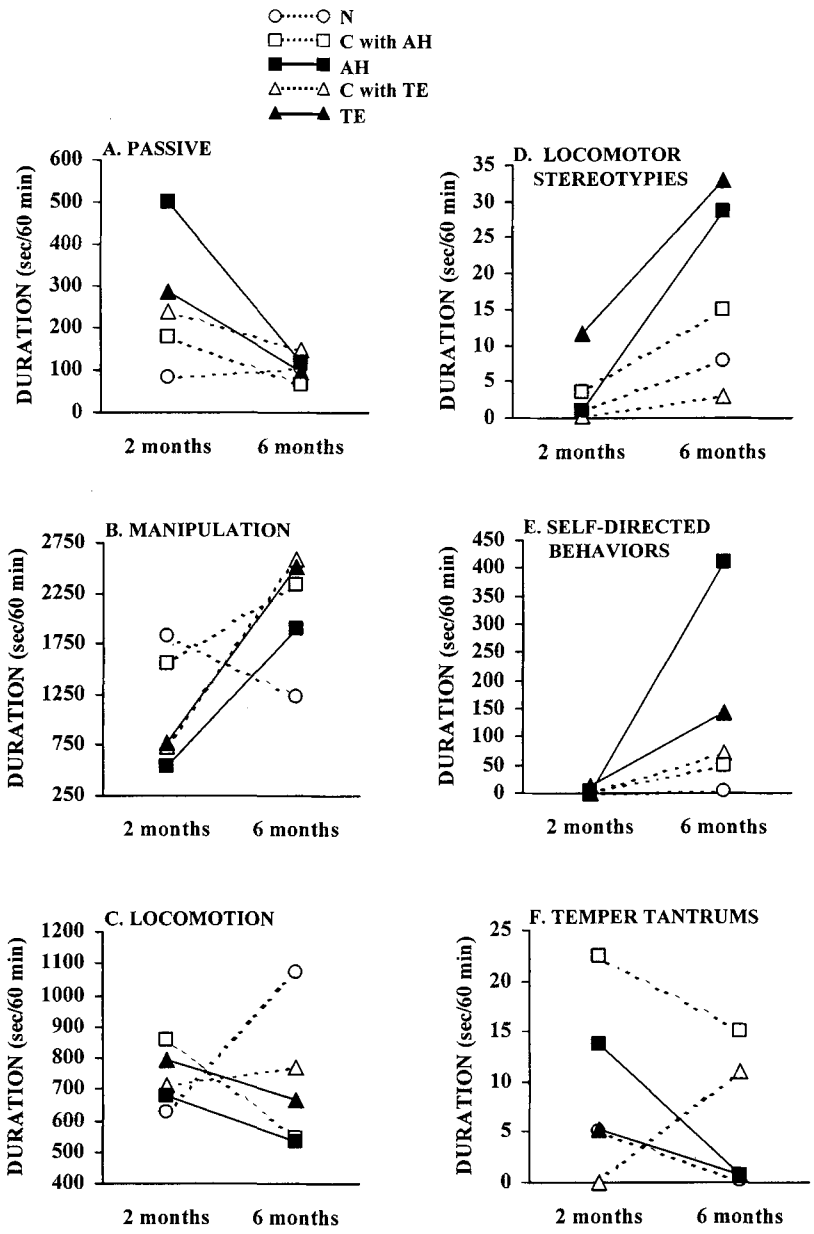

Figure 2. Mean duration of passive (A), manipulation (B), locomotion (C), locomotor stereotypies (D), self-directed behaviors (E), and temper tantrums (F) over the twelve 5-min recording periods (60 min of observation) at both 2 and 6 months of age. N = normal monkeys paired with other normal monkeys; C with AH = unoperated control monkeys paired with monkeys with neonatal medial temporal lobe lesions (AH); C with TE = unoperated control monkeys paired with monkeys with neonatal inferior temporal lesions (TE).

difference was striking for both duration, $t(10) = 2.88$ (Bonferroni adjusted $p < .02$), and frequency, $t(10) = 4.44$ (Bonferroni adjusted $p < .002$). Between the two ages, total social contact increased slightly in the N+N dyads, whereas it decreased markedly in the AH+C dyads: Group × Age interactions for duration, $F(1, 8) = 6.34$, $p < .04$, and frequency, $F(1, 8) = 7.18$, $p < .03$.

TE lesion. At 2 months of age, there was slightly but significantly more total social contact in the TE+C dyads than in the N+N dyads, $t(7) = 2.95$ (Bonferroni adjusted $p < .04$) for frequency. At 6 months, however, the amount of such contact in the TE+C dyads was less than that in the N+N dyads: $t(9) = 4.96$ (Bonferroni adjusted $p < .001$) and $t(9) = 3.74$ (Bonferroni adjusted $p < .005$) for duration and frequency, respectively. Between the two ages, total social contact increased slightly in the N+N dyads but decreased substantially in the TE+C dyads: Group × Age interactions for duration and frequency, $F(1, 7) = 10.46$, $p < .01$, and $F(1, 7) = 28.43$, $p < .001$, respectively.

AH versus TE lesions. Whereas at 2 months of age, the two lesion groups displayed nearly normal amounts of contact, by 6 months, both lesion groups engaged in it far less than Group N. There were no differences between the two groups at either age.

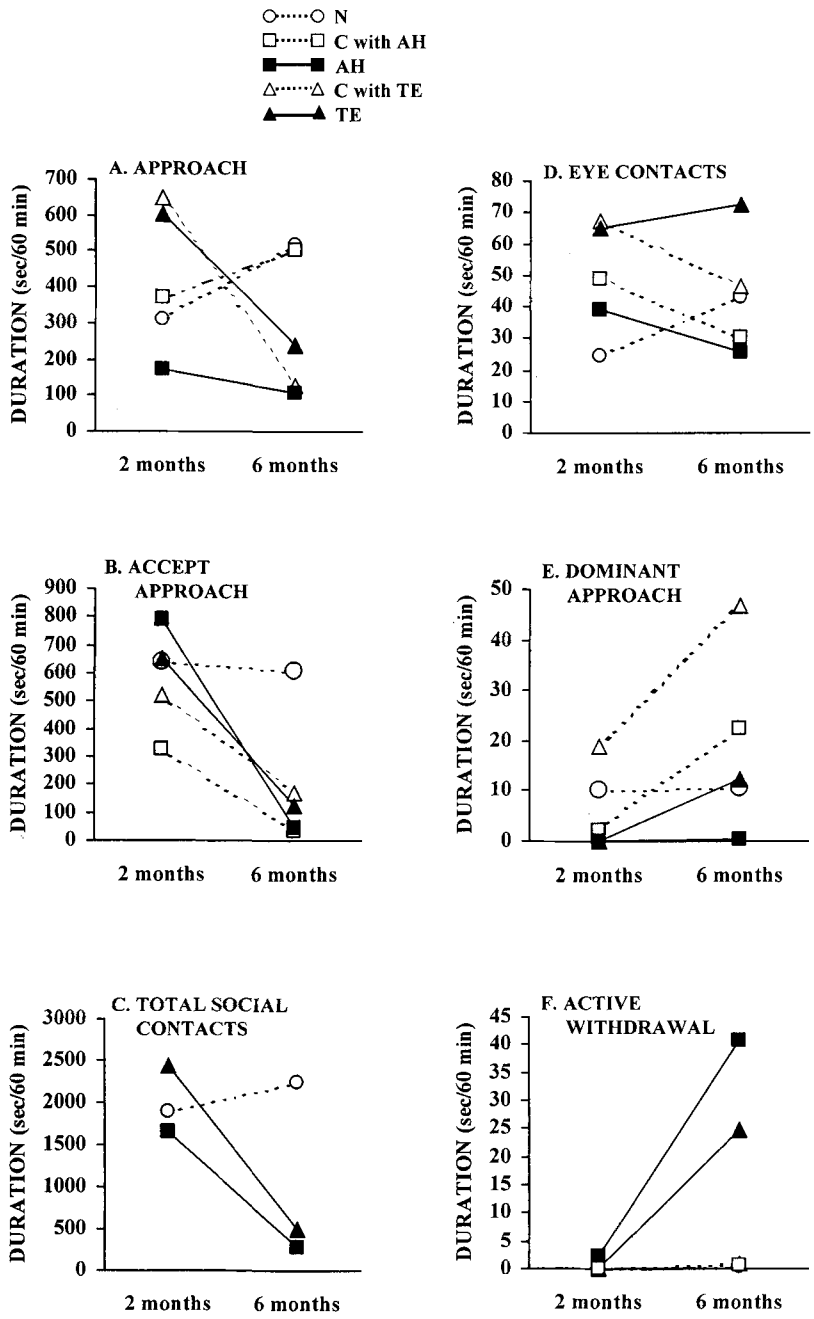

Figure 3. Mean duration of approach (A), accept approach (B), total social contacts (C), eye contacts (D), dominant approach (E), and active withdrawal (F) over the twelve 5-min recording periods (60 min of observation) at both 2 and 6 months of age. N = normal monkeys paired with other normal monkeys; C with AH = unoperated control monkeys paired with monkeys with neonatal medial temporal lesions (AH); C with TE = unoperated control monkeys paired with monkeys with neonatal inferior temporal lesions (TE).

Eye Contact

AH lesion. Initially, eye contact did not differ between groups (see Table 2 and Figure 3D). Later, however, at 6 months of age, the AH+C dyads displayed less eye contact than the N+N dyads: group effects for frequency, $F(2, 21) = 3.70$, $p < .04$ (pairwise comparison AH < N, $p < .08$). This was due to both a decrease with age in the AH+C dyads and an increase in the N+N dyads: Group × Age interactions for duration, $F(2, 17) = 2.81$, $p = .08$.

TE lesion. At 2 months of age, the TE+C dyads displayed more eye contact than did the N+N dyads: group effects for frequency, $F(2, 15) = 7.79$, $p < .005$, and duration, $F(2, 15) = 13.09$, $p < .001$ (pairwise comparisons, $p < .005$ and $p < .03$ for duration and frequency, respectively). At 6 months, eye contact remained unchanged in Group TE, increased in Group N, and decreased in Group C, but the group differences did not reach significance.

AH versus TE lesions. At both ages, Group TE displayed more eye contact than Group AH (TE > AH, $p < .03$, for frequency at both ages).

Dominant Approach

AH lesion. At age 2 months, Group N engaged in dominant approach more than the other two groups, a difference that fell just short of significance: group effect for frequency, $F(2, 17) = 2.83$, $p = .08$ (see Table 2 and Figure 3E). At age 6 months, however, this behavior increased dramatically in Group C: group effect for duration, $F(2, 21) = 8.58$, $p < .002$ (pairwise comparison, C > N and AH, all $ps < .004$), and Group × Age interaction for frequency, $F(2, 17) = 6.61$, $p < .008$. Group AH showed no dominant approach at either age.

TE lesion. At 2 months of age, there were no differences between groups. At 6 months, this behavior remained at the same level as before in Group N, but it increased markedly in Group C: group effect for frequency, $F(2, 19) = 10.22$, $p < .001$ (pairwise comparison, C > N and TE, all $ps < .05$). This difference resulted in a significant Group × Age interaction for frequency, $F(2, 15) = 11.98$, $p < .001$.

AH versus TE lesions. Whereas at 2 months, neither lesion group exhibited dominant approach, at 6 months, Group TE but not AH displayed a normal amount of this behavior (TE > AH, $p < .03$ for frequency).

Active Withdrawal

AH lesion. Unlike dominant approach, active withdrawal was exhibited almost exclusively by the monkeys in Group AH as opposed to their comparison groups, particularly at 6 months: group effect for duration, $F(2, 21) = 11.58$, $p < .000$ (pairwise comparisons AH > C and N, $ps < .003$), and for frequency, $F(2, 21) = 12.11$, $p < .000$ (pairwise comparisons, AH > C and N, $ps < .002$; see Table 2 and Figure 3F). Between the two ages, this behavior increased sharply in Group AH: Group × Age interaction for duration, $F(2, 17) = 20.54$, $p < .000$, and frequency, $F(2, 17) = 6.61$, $p < .008$.

TE lesion. Active withdrawal was also observed in Group TE, but only at 6 months of age: group effect for frequency, $F(2, 19) = 21.68$, $p < .000$, and duration, $F(2, 19) = 18.00$, $p < .000$ (pairwise comparison for both, TE > N and C, all $ps < .000$). In addition, the appearance of active withdrawal in the TE group at 6 months resulted in Group × Age interactions for duration, $F(2, 15) = 757.19$, $p < .000$, and frequency, $F(2, 15) = 74.68$, $p < .000$.

AH versus TE lesions. The increase in active withdrawal between the two ages was greater in Group AH than in Group TE ($p < .04$).

Disturbances of Behavior

Locomotor Stereotypies

AH lesion. Locomotor stereotypies were not evident in any of the three groups during the first assessment (see Table 2 and Figure 2D). At 6 months of age, however, Group AH showed more such stereotypies than either of the other groups: group effect for frequency, $F(2, 21) = 4.55$, $p < .02$ (pairwise comparisons AH > N, $p < .02$), though there were no interactions with age.

TE lesion. There were no group differences at either age. Instead, all groups showed a slight, but nonsignificant, increase in locomotor stereotypies between the two assessments.

AH versus TE lesions. There were no differences between these two groups at either age.

Self-Directed Behaviors

AH lesion. Self-directed behaviors were hardly evident at 2 months but became quite pronounced in Group AH by 6 months of age: Age × Group interaction for frequency, $F(2, 17) = 4.27$, $p < .03$ (see Table 2 and Figure 2E).

TE lesion. Here, too, self-directed behaviors were hardly evident at 2 months but increased at 6 months in Group TE: group effect for frequency, $F(2, 19) = 3.53$, $p < .05$ (pairwise comparison, TE > N, $p = .05$); Group × Age for frequency, $F(2, 15) = 7.48$, $p < .006$.

AH versus TE lesions. Although there were no differences between lesion groups at 2 months, at 6 months the AH group exhibited a greater increase in self-directed behaviors than the TE group ($p < .04$, for frequency).

Temper Tantrums

AH lesion. There were no group differences in temper tantrums at either age (see Table 2 and Figure 2F). However, the monkeys in Group AH did exhibit this behavior at 2 months when they were first placed in the play cage (average frequency of 4.25 during the very first period), whereas neither of the other groups displayed it.

TE lesion. At 2 months, there were no group differences. However, at 6 months, Group C displayed more temper tantrums than the other two groups: group effect for duration, $F(2, 19) = 3.77$, $p < .04$, and for frequency, $F(2, 19) = 3.58$, $p < .05$ (pairwise comparisons for both, C > N, $p = .05$), but the Group × Age interaction fell just short of significance for both duration, $F(2, 15) = 3.31$, $p = .064$, and frequency, $F(2, 15) = 3.04$, $p = .07$.

AH versus TE lesions. Group AH had more temper tantrums than Group TE at 2 months ($p < .02$), although this difference disappeared at 6 months.

Behavioral Activity in the Unoperated Controls

As indicated earlier in the Subjects section, there were four triads consisting of 1 unoperated control monkey, 1 monkey with an AH lesion, and 1 with a TE lesion. Three of these triads were observed in the dyadic pairs AH+C and TE+C at both ages. Comparison of the monkeys in Group C with those in Group N both when the Group C monkeys were paired with the monkeys in Group AH and when they were paired with the monkeys in Group TE revealed several differential effects at the two ages tested. For example, at 2 months of age, the monkeys in Group C had more temper tantrums than those in Group N ($p = .05$ and .04 for duration and frequency, respectively) when the Group C monkeys were observed in AH+C dyads than when they were observed in the TE+C dyads (see Figure 2F). In addition, at the initial assessment, monkeys in Group C had more eye contact than those in Group N ($p = .01$ for duration), and this difference was greater when monkeys in Group C were observed in the TE + C dyads

than when they were observed in the AH+C dyads (see Figure 3D). However, by 6 months of age, the monkeys in Group C had more temper tantrums than Group N, regardless of grouping (see Figure 2F). In addition, at this age, Group C displayed more dominant approach than Group N ($p < .02$) when the Group C monkeys were in the TE+C dyads than when they were in the AH+C dyads (see Figure 3E).

DISCUSSION

The results of the present study confirm earlier findings (Ruppenthal, Walker, & Sackett, 1991) indicating that normal infant monkeys raised in individual cages but given daily socialization periods with age-matched normal peers develop adequate social relationships and no, or negligible, behavioral disturbances. By contrast, in the same rearing environment, monkeys with selective neonatal temporal lobe ablations exhibited severe and widespread socioemotional abnormalities, which included changes in general activity, impaired social skills, and the emergence of behavioral disturbances. The nature and time course of these behavioral changes differed, however, depending on whether the lesions involved the medial temporal lobe or the inferior temporal cortex.

In the following sections, we first consider the effects of the experimental rearing conditions on the behavioral development of normal infant monkeys raised together. We next discuss the behavioral changes following each type of lesion and then relate these changes to those found after similar lesions in adulthood. Finally, we point out possible relationships between the socioemotional abnormalities seen here after selective neonatal temporal lobe lesions in monkeys and those occurring in developmental neuropsychiatric disorders in humans.

Behavioral Activity in the Normal Dyads

Variations among social rearing conditions produce differential behavioral outcomes in the young rhesus monkey (Chamove, Rosenblum, & Harlow, 1973; Champoux, Metz, & Suomi, 1991; Coehlo & Bramblett, 1982; Novak & Harlow, 1975). Thus, although total or partial social isolation of individually reared infant monkeys yields severe deficits in the formation and maintenance of social bonds and the regulation of emotions (Capitanio, 1986; Harlow & Harlow, 1962; Suomi, 1982), short periods of daily social contacts with peers appear to be sufficient to promote species-typical behavioral patterns in individually caged infant macaques (Rosenblum, 1961; Sackett, 1982; Schneider & Suomi, 1992; for a review, see Suomi, 1997). Indeed, Ruppenthal et al. (1991) demonstrated that infant primates separated from their mothers at birth develop more normally if caged singly and given short periods of socialization than if they are kept in continuous social contact with age-matched peers. Results consistent with this finding were obtained in the present experiment. Mother-separated normal infant monkeys reared in individual cages and given daily social interactions with peers (Group N) developed few, if any, behavioral disturbances, and most aspects of their social and emotional development generally mimicked species-normative patterns. Nevertheless, even under these optimal peer-rearing conditions, mother-separated monkeys are in general more reactive to biobehavioral responses and more impulsive than monkeys born and raised in natural habitats (for a review, see Suomi, 1997). Thus, it is important to bear in mind that the effects of the selective neonatal temporal-lobe lesions on emotional responses and social skills could have differed from those reported here had the monkeys been raised under more natural conditions.

Effects of Neonatal Medial Temporal Lesions

In contrast to the relatively normal development of a complex social behavioral repertoire seen in the normal monkeys (Group N), prominent behavioral changes that became progressively more severe were found in monkeys with neonatal lesions of the medial temporal lobe (Group AH). First, early medial temporal lesions yielded transient changes in general activity. Thus, at 2 months of age, the operated monkeys displayed less exploratory behavior than normal controls, as reflected in their greater passivity and lesser manipulation of objects in their surroundings. These changes were transient, however, in that they were no longer apparent when the operated monkeys reached 6 months of age.

In addition to changes in general activity, the early medial temporal lesions led to severe alterations in the development and maintenance of social bonds. As early as 2 months of age, the monkeys in the AH group initiated fewer social contacts than either type of normal control, although they still accepted the social approaches attempted by the unoperated monkeys. They also displayed a normal amount of eye contact and dominant approach. Thus, at this early age, the time they spent in social interactions were in the normal range, although the unoperated control monkey in the pair was more active in initiating social interactions. Four months later, however, social interactions in the AH+C dyads decreased dramatically. Not only did the operated infant monkeys initiate fewer social contacts than the unoperated controls, they also withdrew more often from the numerous social attempts of the unoperated controls. Further, they displayed less eye contact than the normal monkeys (Group N). This pattern of results indicates that the monkeys in the AH group were not simply socially inept and uninterested in social contact but actively avoided such contact. Their lack of social skills was also reflected in qualitative differences between them and their peers in social signals conveyed through facial and postural actions that were readily noted, though not quantified, by the observers. For example, the operated infant monkeys had blank, unexpressive faces and failed to show the normal pattern of playful body posturing.

Finally, the neonatal medial temporal lesions resulted in a progressive increase in many behavioral disturbances, such as irritability, locomotor stereotypies, and self-directed activities. Unlike the unoperated controls, monkeys in the AH group displayed distress reactions when first placed in the play cage at 2 months of age, and then, at 6 months of age, showed far more stereotyped behaviors, such as rocking, self-holding, and crouching.

The behavioral changes seen after early medial temporal lesions resemble those reported after similar lesions, particularly amygdalectomy, incurred in adulthood. Thus, amygdalectomy in adult monkeys results in a short-lasting increase in passivity (Weiskrantz, 1956), a decrease in aggression and social proximity, as well as a fall of status in the social hierarchy (Dicks, Myers, & Kling, 1969; Rosvold, Mirsky, & Pribram, 1954; for a review, see Kling & Brothers, 1992) and a reduction in vocal and postural threat behavior (Kling, Dicks, & Gurowitz, 1968). Despite the similarities in the effect of early and late damage to the medial temporal lobe, there were also marked differences. For example, there were no instances in which monkeys in the AH group

engaged in coprophagy or excessive sexual behavior during the first 6 months of life as is often observed after equally extensive lesions in adults (Kling & Brothers, 1992; Kling & Dunne, 1976; Klüver & Bucy, 1938; 1939). Further, in a study designed to measure the effects of early medial temporal lesions on emotional reactions to novel stimuli, including normally fearful objects (Nalwa & Bachevalier, 1991), it was found that, at 9 months of age, monkeys in the AH group failed to show the loss of fear and the hyperorality typically seen in adults given the same lesions (Klüver & Bucy, 1938, 1939; for a review, see Kling & Brothers, 1992). Conversely, none of the stereotypic behaviors found here in the neonatally operated monkeys were observed in monkeys given the same lesions in adulthood (for a review, see Kling & Brothers, 1992).

Although additional behavioral changes in the monkeys with the early AH lesions might have been expected after further maturation, thereby resulting in greater similarity to the behavioral pattern observed in adult monkeys given the same lesion, our preliminary findings (Málková, Mishkin, Suomi, & Bachevalier, 1997) suggest otherwise. In this later study, we compared social interactions in five groups of monkeys ages 5–7 years. These included three groups from the present experiment (Groups N, AH, and C) and two new groups, one consisting of monkeys given AH lesions in adulthood and the other, their age-matched unoperated controls, both groups having been reared under the same conditions as the others. All monkeys were tested in dyadic social interactions in a large enclosure according to the same procedures as those described in the present experiment. We found not only that the socioemotional abnormalities produced by the early medial temporal lesions were long-lasting but also that the magnitude of these abnormalities when the monkeys reached adulthood was far greater than that produced by the late medial temporal lesions. In addition, whereas the adult monkeys with early lesions continued to exhibit behavioral stereotypies, those with late lesions showed none.

The socioemotional abnormalities observed in monkeys with early medial temporal lesions are not surprising if one considers the substantial evidence on the role played by the amygdala especially in the regulation of emotional states and the maintenance of social relationships in monkeys (for reviews, see Aggleton, 1992; Emery & Amaral, 2000). Indeed, behavioral changes qualitatively similar to those described here after early medial temporal lesions had already been reported by Thompson and his collaborators after early lesions restricted to the amygdala (Thompson, 1969, 1981; Thompson et al., 1969; Thompson & Towfighi, 1976). These investigators had demonstrated that, compared with their unoperated controls, monkeys amygdalectomized in early infancy exhibited a transient increase in passivity and a loss of social interactions that became more profound as the monkeys matured. These findings suggest that the abnormalities in general activity and social behavior found in our AH group could be attributable to amygdala damage alone. Nevertheless, preliminary data on the behavioral effects of early, partial, medial temporal lesions (Bachevalier, 1994; Beauregard, Málková, & Bachevalier, 1995) indicate that medial temporal structures other than the amygdala also contribute significantly to the regulation of socioemotional behavior. First, although early damage to the amygdaloid complex and adjacent cortex resulted in a pattern of socioemotional effects almost identical to that found after the complete AH lesion, the magnitude of the effects was less. Second, although early damage to the hippocampus and adjacent cortex did not result in significant socioemotional changes in early infancy (Bachevalier, 1994), they did yield a significant loss of social interactions and the appearance of locomotor stereotypies when the monkeys reached adulthood (Beauregard et al., 1995). This pattern of results suggests that the hippocampus may well contribute to the regulation of socioemotional behavior, and, further, that the effects of damage to it may be greater when the damage occurs in early infancy than when it occurs in adulthood (Bayer, Brunner, Hine, & Altman, 1973; Beauregard et al., 1995; Lipska et al., 1995; Meunier, Bachevalier, Murray, Merjanian, & Richardson, 1991; Mickey, Ferguson, Nemeh, Mulvihill, & Alderks, 1989).

We reported earlier that the monkeys with neonatal medial temporal lesions had memory deficits strikingly similar to those found in adults with the same lesions (Málková et al., 1995). The findings suggested that compensatory mechanisms do not always operate to produce recovery of function after early brain damage. In the case of socioemotional behavior, however, the behavioral deficit after neonatal medial temporal lesions not only was more severe than that found after late lesions but also was accompanied by abnormal behaviors that had never been reported in adult monkeys given this same lesion (Málková et al., 1997). The comparison suggests that the monkeys operated in adulthood retained at least some aspects of the socioemotional repertoire they had acquired during maturation, whereas the neonatally operated monkeys never succeeded in acquiring them. Supporting this suggestion is the finding that the original dyads containing monkeys with early medial temporal lesions did not show the increase in social interaction from infancy to adulthood that was observed in the normal dyads. Furthermore, compared with the recovery of normal socioemotional responses seen after early damage to Area TE, the severe behavioral changes displayed by monkeys with early AH lesions suggests that any neural reorganization that occurs after this particular type of neonatal lesion may be more harmful than beneficial, perhaps because it disrupts the functioning of late-maturing neural systems (Isaacson, 1984; Isaacson, Springer, & Ryan, 1986; Lipska et al., 1995). This view is supported by recent data in monkeys demonstrating that, unlike late damage to the medial temporal lobe, early damage to it interferes with the functions of a neural system remote from the injury, namely, the dorsolateral prefrontal cortex (Bertolino et al., 1997) and the anatomically related portion of the neostriatum (Chlan-Fourney, Webster, Felleman, & Bachevalier, 2000; Saunders, Kolachana, Bachevalier, & Weinberger, 1998). As discussed below, these experimental findings may have important implications for socioemotional as distinguished from other types of behavioral and cognitive development after medial temporal damage in children.

Effects of Neonatal Inferior Temporal Lesions

The socioemotional effects of early inferior temporal lesions (Group TE) were in general milder than those observed after early AH lesions. Thus, although both types of lesion induced passive behavior at 2 months of age, the passivity was substantially less after the TE lesion (a mean of 287 s/60 min) than after the AH lesion (a mean of 504 s/60 min). Similarly, although total social contacts at 6 months of age decreased sharply after both lesions, the TE group did not exhibit a complete loss of the social repertoire. For example, unlike the AH group, the TE group had normal

amounts of eye contact and dominant approaches and showed less active withdrawal. Thus, although the monkeys with early area TE lesions did not develop strong affiliative bonds with their unoperated controls, they did show some of the normal complex of social behavioral responses. Also unlike the AH lesions, the TE lesions did not result in behavioral disturbances; the amount of self-directed behaviors they displayed was in the same range as that shown by the normal monkeys (Group N).

Interestingly, our preliminary findings indicate that when retested as adults, monkeys with early TE lesions exhibit normal amounts of social contact and no significant behavioral disturbances (Málková, Bachevalier, Kirkpatrick, Merjanian, & Mishkin, 1991). Thus, as compared with the severe and permanent behavioral abnormalities seen after early lesions to the medial temporal lobe, the changes in socioemotional behavior after early Area TE lesions were only mild and transitory. Nevertheless, it is worth noting that because the early temporal cortical Area TE lesions also included portions of the perirhinal cortical Area 36 (lateral to the rhinal sulcus), it is possible that damage to the perirhinal cortex could be responsible, either by itself or in combination with Area TE damage, for the mild behavioral deficit observed. This possibility needs further investigation.

Both the short- and long-term socioemotional consequences of early TE lesions also appear to be relatively modest compared with those seen after late anterolateral temporal cortical ablations. Such adult lesions typically lead to oral behavior, hyperreactivity to stimuli, and decreased emotionality (Horel et al., 1975; Horel & Misantone, 1974; Iwai et al., 1986), as well as to significant alterations in social behavior and affect, including decreases in allogrooming, facial expressions, vocalizations, maternal behavior, and sexual behavior, among others (Franzen & Myers, 1973; Meyer, 1972; Myers & Swett, 1970). In all previous reports but one (Iwai et al., 1986), the anterolateral temporal lesions included not only most of Area TE but also the cortex of the temporal pole, an area that, like the amygdala, appears to play a significant role in the regulation of socioemotional behavior. Because the temporal pole was not included in the early TE lesions of the present experiment, the difference between their effects and those of late anterolateral temporal lesions could be due either to the sparing of temporal polar cortex in our monkeys or to a greater compensatory response of the brain after early than after late TE lesions, or to both.

If the relative preservation of socioemotional behavior after early as compared with late TE lesions were to prove correct, the finding would parallel the relative preservation of visual learning and memory abilities reported earlier in our neonatally operated monkeys (Bachevalier et al., 1990; Bachevalier & Mishkin, 1994; Málková et al., 1995). The latter results indicate that early neural plasticity allows other neural tissue to compensate for the neonatal loss of Area TE. The regulation of emotional responses and social affiliation is thought to be related in part to a neural system linking the higher order sensory areas of the neocortex, such as Area TE (the anterior portion of the inferior temporal visual area) to the amygdala (Aggleton & Mishkin, 1986). According to this notion, visually mediated socioemotional functions could persist in the absence of Area TE only if the amygdala were to receive inputs from visual areas caudal to TE, such as Area TEO. Although TEO does not project to the amygdala in adult monkeys, this area does send transient projections to the lateral and basolateral nuclei of the amygdala in infant monkeys (Webster, Ungerleider, & Bachevalier, 1991a), and, interestingly, these transient projections are maintained after early damage to Area TE (Webster, Ungerleider, & Bachevalier, 1991b). These persisting projections could thus provide a pathway through which visual information is transmitted to the amygdala and thereby account for a relative preservation of visually mediated social skills.

Behavioral Activity of the Unoperated Controls

The unoperated controls (Group C) appeared to adapt to the behavioral changes of their operated peers, as indicated by the difference between amount of social contact they attempted and the amount engaged in by the monkeys of Group N. Thus, Group C monkeys paired with the monkeys in Group AH engaged in less social behavior (a mean 796 s/60 min) than the monkeys in Group N (a mean of 2,248 s/60 min). Whether unoperated controls raised with monkeys given AH lesions will still display normal social contacts in C+N dyads remains to be explored. However, informal observations made on several occasions in which Group C monkeys belonging to the AH+C dyads were paired together (i.e., C+C) did reveal relatively normal play behavior. In addition, when the TE+C dyads were retested as adults, the monkeys in Group C displayed normal amounts of social contact, suggesting that, earlier, they had learned to respond to the temporarily aberrant behavior of Group TE monkeys but that they were not permanently affected. This notion is further supported by the behavioral responses of those Group C monkeys that were observed in both AH+C and TE+C dyads. When placed with the Group TE monkeys at 6 months of age, they exhibited more dominant approaches than when they were placed with Group AH monkeys at this age. Why the comparatively mild behavioral effects in monkeys with TE lesions seem to have affected the unoperated controls more than the severe abnormalities in monkeys with AH lesions is unclear. One possibility, however, is that the complete loss of social skills in the latter monkeys and, more importantly, their frequent withdrawal from social contact, was less disruptive for the unoperated controls than the aberrant social interactions displayed by the monkeys with early TE lesions.

Relationship to Developmental Disorders in Humans

There are several clinical reports indicating that temporal lobe damage early in life can result in profound alterations of behavior. The constellation of behavioral abnormalities commonly referred to as the Klüver–Bucy syndrome has been reported in children suffering from herpes encephalitis (Chutorian & Antunes, 1981), hypoxia (Tonsgard, Harwicke, & Levine, 1987), bitemporal arachnoid cysts (Rossitch & Oakes, 1989), and unilateral left temporal oligodendroglioma (Hoon & Reiss, 1992). In the last case, the damaged areas included the amygdala, entorhinal cortex, parahippocampal gyrus, and a portion of the hippocampus, and this neuropathology was reported to have resulted in mild to moderate mental retardation in the child, together with myriad abnormalities in social and affective behavior as well as hyperactivity and irritability. The child was described as suffering from autism, because his behavioral symptoms met the *Diagnostic and Statistical Manual of Mental Disorders* (3rd ed., Rev. [*DSM–III–R*]; American Psychiatric Association, 1987) criteria for pervasive developmental disorder. The major criteria for autism in this manual include impairment in reciprocal social interactions, in

verbal and nonverbal communication, and in imaginative activity, together with a markedly restricted repertoire of activities and interests and the display of stereotypies. Although not included in the *DSM–III–R* criteria for autism, mental retardation co-occurs with autism in approximately two thirds of the cases (Rutter, 1970). Interestingly, autistic behavior has also been reported in cases of tuberous sclerosis associated with pathology in the medial temporal region (Bolton & Griffiths, 1997; Deonna, Ziegler, Moura-Serra, & Innocenti, 1993); neurofibrillary tangles in the amygdala, entorhinal cortex, and perirhinal cortex (Hof, Knabe, Bovier & Bouras, 1991); and partial absence of the left temporal lobe (White & Rosenbloom, 1992). Furthermore, postmortem neuropathology of the limbic system, including the amygdala, hippocampus, and surrounding cortical areas, was found in all six autistic cases investigated by Bauman and Kemper (1985, 1988, 1994). Magnetic resonance imaging studies of the medial temporal region in autistic individuals have revealed disproportionately large hemispheric white-matter volumes in the temporal region (Filipek, 1996), increased amygdala–hippocampal boundary tissue (Abell et al., 1999; Reiss, Lee, & Freund, 1994), and decreased amygdala volumes (Aylward et al., 1999), although normal hippocampal volumes were found in several autistic cases (Piven, Bailey, Ranson, & Arndt, 1998; Saitoh, Courchesne, Egaas, Lincoln, & Schreibman, 1995). Finally, a recent functional neuroimaging study (Baron-Cohen et al., 2000) reported dysfunction of the amygdala in people with autism and Asperger's syndrome.

In sum, there is now substantial clinical evidence suggesting that medial temporal pathology in infancy can result in autistic behavior. This proposal, which has been advanced by others (DeLong, 1978; DeLong, Bean, & Brown, 1981; Fein, Pennington, & Waterhouse, 1987; Hetzler & Griffin, 1981), draws support from the present experimental results. Comparison of the behavioral alterations in autistic children with those in infant monkeys given neonatal medial temporal lesions reveals many striking similarities (Bachevalier, 1994). Both show an absence of social interactions, a lack of normal facial and body expressions, and numerous behavioral stereotypies. Also in both, the disorder becomes fully apparent only after early infancy, but once it does emerge fully it remains permanent. Thus, both the time course and the nature of the behavioral abnormalities in autistic children and in monkeys with neonatal medial temporal lesions are sufficiently close to encourage further investigation of the involvement of the medial temporal lobe in this debilitating human development disorder.

With regard to the inferior temporal cortex, no reports have yet appeared of early selective damage to the analogous cortical visual tissue in humans. Nevertheless, on the basis of the moderate increase in the general activity of the monkeys with early TE lesions, as well as their tendency to shift rapidly between behavioral activities, together with the disturbed behaviors they evoked in the unoperated control monkeys with which they were paired, we have suggested earlier (Merjanian, Bachevalier, Pettigrew, & Mishkin, 1989) that early TE lesions produce behavioral changes resembling those seen in children with attention-deficit hyperactivity disorder. This possible relationship too warrants further study.

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