Reactions to Familiar and Novel Objects in Infant Monkeys With Neonatal Temporal Lesions

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ABSTRACT: Adult monkeys with late temporal lobe damage are known to touch and mouth objects compulsively, even unknown objects. To determine whether infants with early temporal damage display this symptom as well, 9-month-old rhesus monkeys with neonatal ablations of either the medial temporal lobe or inferior temporal cortex were exposed to four objects, two familiar and two novel. All operated infants were less active/more withdrawn than controls and showed neither exaggerated object manipulation nor hyperorality. Furthermore, like controls, they touched novel objects less than they touched familiar ones. Thus, infants with neonatal medial or inferior temporal ablations did not display the compulsive exploration evidenced after similar lesions in adulthood and retained some ability to detect novelty despite their known memory impairments. *Hippocampus 2003;13:489–493.*

KEY WORDS: amygdala; hippocampus; inferior temporal cortex; emotion; memory

In earlier studies, peer-raised infant monkeys having incurred bilateral aspiration of either the medial temporal lobe (amygdala, hippocampus, and surrounding cortex; MTL) or the visual inferior temporal cortex (area TE) during the first month of life were found to present with memory deficits and an impoverishment of dyadic social interactions with normal peers that were qualitatively similar by 1 year of age (despite differences in magnitude) to those seen after equivalent lesions sustained in adulthood (e.g., Málková et al., 1995; Bachevalier et al., 2001). The question addressed in the present report is whether these same infants exhibit still another of the hallmark symptoms after temporal insult in maturity, that is, an excessive manual and oral exploration of objects, both known and unknown alike (e.g., Klüver and Bucy, 1939; Horel et al., 1975). To this end, 9-month-old infants with neonatal MTL or TE removal, and their unoperated peers, were exposed to four objects, two highly familiar and two novel. The animals were observed individually while placed in a testing apparatus; this was done because hyperresponsiveness to objects emerges most clearly in isolation after late temporal damage (Kling and Brothers, 1992) and probably after early temporal damage as well (Thompson, 1969; Thompson and Towfighi, 1976; Prather et al., 2001).

The subjects were 16 rhesus monkeys (*Macaca mulatta*) that had been nursery-reared at the Laboratory of Neuropsychology, National Institute of Mental Health (NIMH), Bethesda, Maryland, in social dyads or triads since the day after their birth. Three monkeys (one male, two female) had sustained neonatal MTL removal, and three (two male, one female) neonatal TE removal. The remaining 10 monkeys (five male, five female) were unoperated controls, six peer-raised with each other (group N) and four peer-raised with one or two operated animals (group C). The present study took place at 9 months of age, after assessment of visual preference for three-dimensional (3D) objects at 5–30 days of age (Bachevalier et al., 1993), visual discrimination learning at 3 months (Bachevalier et al., 1990), and social interactions with peers at 2 and 6 months (Bachevalier et al., 2001). Rearing conditions, surgery (performed in two stages at 1 and 3 weeks of age), and lesion extent (evaluated when the monkeys were about 7 years) have been detailed in these previous reports. The present operated animals correspond to cases AH 5–7 (AH was the former designation for MTL) and TE 6–8 in all earlier studies (see also Bachevalier and Mishkin, 1994). All MTL removal included the amygdala and all but the most caudal 1–2 mm of the hippocampal formation, together with the periamygdaloid, entorhinal, and parahippocampal cortex. Unintended damage was restricted to the fundus of the rhinal sulcus (perirhinal area 35) and the ventralmost portion of visual area TEO. All TE removal encompassed the anterior two-thirds of the inferior temporal gyrus, ending at the fundus of the superior temporal sulcus, dorsally, at the fundus of the occipitotemporal sulcus, ventrocaudally, and 1–2 mm lateral to the lateral lip of the rhinal sulcus, ventrorostrally (thus sparing most of perirhinal area 36). Unintended damage was limited to the rostralmost portion of area TEO and occurred only in TE 8.

The infants were tested in an adaptation of the task used to assess curiosity and general activity in nursery-reared infant squirrel monkeys (Roy et al., 1981). Reac-

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TABLE 1.

Behavioral Activities
Withdrawal
Suck (finger or toe)
Passive (motionless, except for vocalization or suck)
Abnormal postures (self-hug, face press, crouch, prone)
Motor activities
Normal locomotion (e.g., walking, climbing)
Locomotor stereotypies (e.g., circling, hopping)
Exploration, manual or oral, of the cage and apparatus
Object-directed activities
Approach (look and/or move toward)
Retreat (look and/or move away)
Touch
Mouth (with or without touch)
Aggression (throwing or shaking)
Communication
Facial expression (grimace, lip smack, threat)
Vocalization (cooing, eeing)
Temper tantrum

tions to two familiar and two novel objects were video-recorded while the animal was in a reduced-scale Wisconsin General Testing Apparatus located outside the nursery. The two familiar objects were taken from the animals' daily environment, consisting of a transparent nursing bottle and a pink cotton towel, normally provided to the animal for feeding and contact comfort, respectively. A plastic orange ashtray and a white-and-blue child thong sandal were selected as novel objects. Testing consisted of six daily sessions during which the four objects were presented one at a time, always in the same order (bottle, ashtray, towel, sandal), for 180 s each with 30-s inter-object intervals. One observer, blind with respect of the lesions, analyzed the videotapes, and recorded the frequency and duration of 14 behavioral activities that were then grouped in four categories (Table 1). Scores were examined using analysis of variance (ANOVA), with repeated measures when dictated, followed by Tukey pairwise comparisons. The two unoperated groups did not differ significantly and were therefore pooled into a single N/C group. Also, because only the measure "Touch" varied across sessions (see below), subsequent analyses were performed on mean scores over the six daily sessions.

Overall behavioral patterns (irrespective of object type)

Scores averaged over all four objects showed between-group differences for all behavioral categories except communication. Operated infants spent more time than controls in activities denoting withdrawal from the environment [duration: $F = 11.4$, df (2,13), $P = 0.001$; MTL vs N/C, $P = 0.03$, TE vs N/C, $P = 0.002$], presenting primarily either excessive abnormal postures (five cases) or exaggerated sucking (MTL-7; Fig. 1A). As a corollary, they engaged less often in motor activities [frequency: $F = 11.1$, df (2,13), $P = 0.002$, MTL vs N/C, $P = 0.008$, TE vs N/C, $P = 0.007$], notably exhibiting fewer bouts of environmental exploration (manual or oral) than controls (Fig. 1B). Object-directed activities tended to be diminished as well [frequency: $F = 3.7$, df (2,13), $P = 0.05$; duration: $F = 4.9$, df (2,13), $P = 0.03$; MTL vs N/C, $P > 0.10$; TE vs N/C, $P = 0.03$]. Object mouthing was rare in all operated infants. Object touching was decreased, strikingly in the two male TE cases, and more mildly in the three MTL cases (Fig. 1C). Touch in the latter cases was normal on days 1 and 2 (MTL: 32 ± 8 vs N/C: 36 ± 6 s) but decreased on days 5 and 6 (MTL: 1 ± 0.5 vs N/C: 32 ± 8 s per presentation). No instance of excessive exploration was recorded throughout the course of the study.

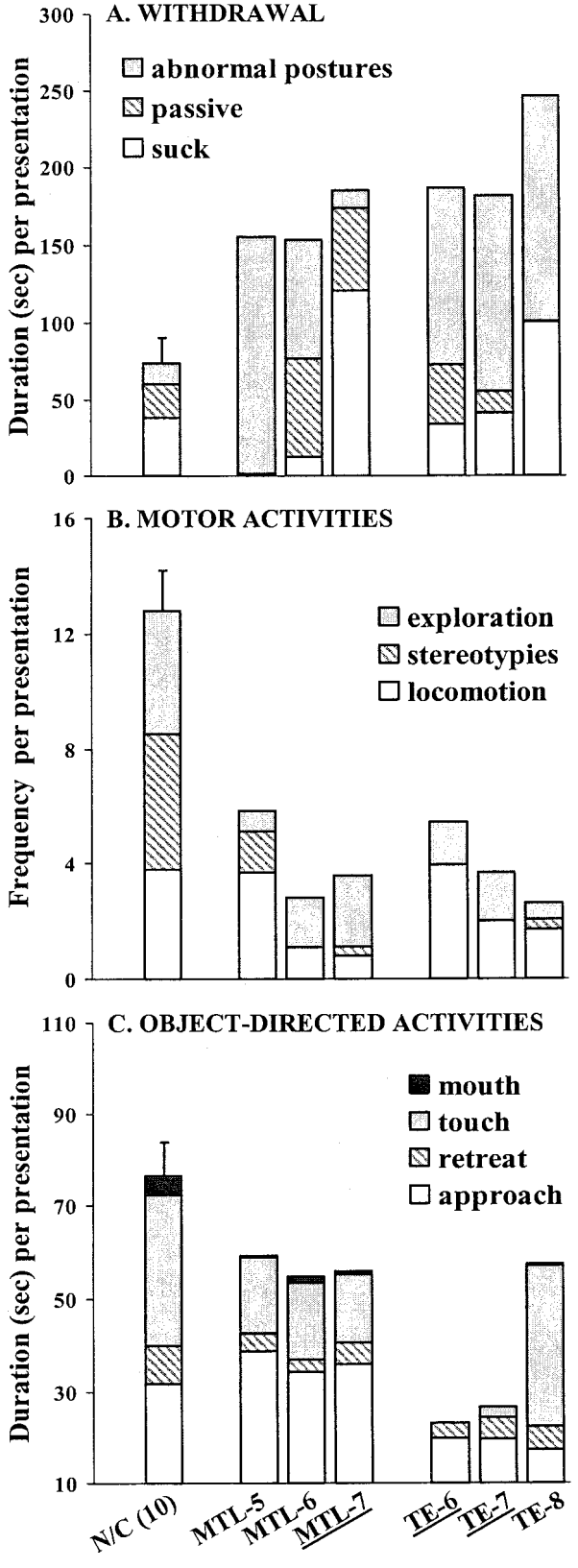
Novelty Effect

Comparisons of category scores for novel versus familiar objects indicated that object type had a reliable effect only on object-directed activities, decreasing in response to novelty [duration: $F = 30.8$, df (1,13), $P < 0.001$], comparably in all groups (Fig. 2). In addition, analyses for each individual activity showed that all infants touched novel objects less than they touched familiar objects [duration: $F = 14.7$, df (1,13), $P = 0.002$]; they also directed their rare facial expressions selectively to familiar objects [frequency: $F = 8.6$, df (1,13), $P = 0.01$].

These results show that when individually and formally exposed to objects at 9 months of age, peer-raised infant monkeys with neonatal MTL or TE ablations were more withdrawn/less active than their unoperated peers, displayed none of the hyperresponsiveness to objects evidenced after temporal lesions in maturity, and interacted less with novel than with familiar objects, as did controls.

Two explanations may account for the absence of exaggerated object exploration in infants with neonatal TE removal. First, late lesions yielding this symptom generally included not only area TE, but the adjacent temporal pole as well (e.g., Horel et al., 1975). It is possible that larger early removal would have enhanced exploration. Second, neonatal TE ablation was previously found to yield minimal mnemonic impairments (Málková et al., 1995) and a social impoverishment that recedes with maturity (Bachevalier et al., 2001), that is, much less severe disorders than those after equivalent lesions in adulthood. The present finding might thus be further evidence of the considerable sparing of function that follows early injury relative to late TE injury. Unpublished data (Fig. 3) obtained with a task assessing adult monkey responses to a battery of emotionally arousing items (Meunier et al., 1999; Meunier and Bachevalier, 2002) suggest that both explanations may hold true. First, monkeys with late TE ablation sparing temporal polar cortex exhibited only a mild exploration increase, indicating that TE damage is indeed insufficient to produce the drastic change reported in the literature (e.g., Horel et al., 1975). Second, the one (male) case with early TE removal assessed in adulthood showed as little exploration as the present infants, suggesting that the compensatory brain reorganization known to follow neonatal TE injury durably prevents hyper-responsiveness. Further studies are needed to confirm these proposals and also to understand why

neonatal TE (or MTL, see below) insult can lead to opposite symptoms, viz. poor object exploration and excessive withdrawal from the environment, as compared with late damage.



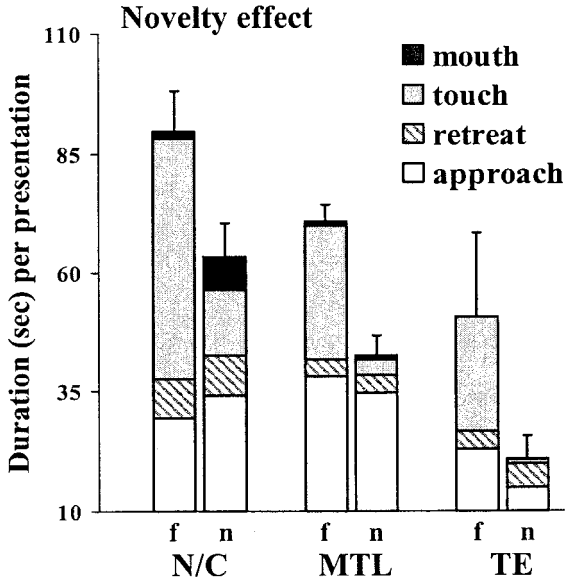


FIGURE 2. Novelty effect. Object-directed activities (i.e., data from Fig. 1C) expressed as mean group scores (duration) per 180-s presentation and calculated separately for the two familiar (f) and the two novel objects (n). Other conventions as in Fig. 1.

In infants that underwent neonatal MTL removal, the absence of hyperresponsiveness cannot be attributed to insufficient lesion extent because damage to the sole amygdala in mature animals can produce this symptom (Meunier et al., 1999). This absence is therefore specific to early MTL damage. It may also be long-lasting (Fig. 3). Indeed, in the emotional task discussed above, monkeys that underwent late MTL removal touched and mouthed the target items excessively, whether they found the objects attractive or aversive; they also explored the cage and apparatus exaggeratedly (not illustrated). By contrast, among the two cases with early MTL removal assessed in adulthood, one (a female) displayed almost no exploration at all, and the only sign of abnormal responsiveness in the other (a male) was a series of brief touching bouts in presence of the rubber snake; hyperorality and exaggerated environment exploration were absent in both cases. In line with these findings, the exploration enhancements previously described in (individually observed) monkeys with neonatal amygdala lesions appear both less drastic and less ubiquitous than those following late amygdala lesions. Prather et al. (2001) reported five exploration bouts per

FIGURE 1. Overall behavior. Scores per 180-s presentation, averaged across the two familiar and two novel objects, for each of the behaviors (except aggression, which almost never occurred) composing the categories: Withdrawal (A, duration), motor activities (B, frequency), and object-directed activities (C, duration). N/C, mean scores of the 10 unoperated infants; MTL 5–7, individual scores of the three infants with neonatal medial temporal lobe ablations; TE 6–8, individual scores of the three infants with neonatal inferior temporal cortex ablations. Note that, because activities were not mutually exclusive (e.g., passivity and suck can co-occur), duration scores cumulated within or across categories can exceed 180 s. Underlined cases denote male operated animals. Error bar represents SEM for the total category score.

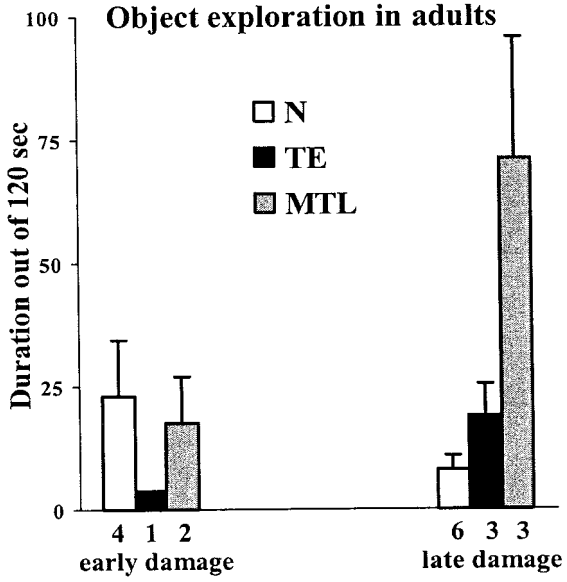


FIGURE 3. Manual and oral exploration of objects in individually observed adult monkeys after temporal damage sustained either in infancy or in maturity. Scores are durations obtained with the task described previously (Meunier et al., 1999; see also Meunier and Bachevalier, 2002) and cumulated over one 20-s presentation of a taxidermic monkey head, one 20-s presentation of a rubber snake, and four consecutive 20-s presentations of a junk object that the animals had to displace to retrieve a food reward (total: 120 s). The three cases with early medial (MTL) or inferior (TE) damage are different from those included in the present study, but they had sustained similar lesions and were raised in the same conditions (see cases TE 1, and AH 1–2 in, e.g., Bachevalier and Mishkin, 1994). Except for more extensive encroachment onto perirhinal area 36, late temporal ablations were comparable to their early counterparts. Note the reduced (TE) to normal (MTL) exploration of animals with early damage (relative to unoperated controls with which they were peer-raised), which contrasts with the slightly (TE) to markedly (MTL) enhanced exploration of animals with late damage (relative to unoperated controls similarly born and raised in U.S. breeding colonies or in the wild). Numerals indicate the number of cases per group.

60 s in infants with early neurotoxic amygdala damage versus one in controls. Thompson (1969) obtained a 40% exploration score (8/20 min) in juveniles with early amygdala aspiration versus 20% (4/20 min) in controls. Both increases seem modest in light of the 70% exploration score (42/60 s), versus 1% (0.7/60 s) in controls, reached by adults with late amygdala aspiration exposed to a rubber snake (Meunier et al., 1999). Also, after early amygdala damage, changes emerged only in the animal's home cage (Prather et al., 2001) or after 24 h in a test cage (Thompson, 1969). In the standard testing situation routinely used to demonstrate late lesions effects, juveniles with amygdala aspiration were, like the present infants, overly passive with no sign of hyperresponsiveness (Thompson, 1969). Taken together, present and past results suggest that (1) hyperresponsiveness to objects is less frequent after early than after late MTL injury, and when it does occur, remains less marked, and (2) early MTL injury can lead to opposite symptoms, viz. excessive withdrawal and hypo-exploration, which are seldom encountered after late damage. Neonatal MTL removal was already known to have slightly less severe consequences on memory than late removal, while having more deleterious effects on dyadic social interactions (Málková et al., 1995, 1997; Bachevalier et al., 2001). The present study complements these findings by demonstrating their differential effect on exploration. Future studies will need to ascertain the relevance of these differences to human syndromes, and notably to determine whether the excessive withdrawal observed here could constitute another resemblance between infant monkeys with early MTL damage and human children with autistic disorders.

Finally, one interesting finding of the present study is the appropriate decrease in object-directed activities displayed by all operated infants in response to novelty. This effect, predictable for TE cases in light of their minimal memory impairments (Málková et al., 1995), is more unexpected for MTL cases, which suffer from marked deficits in visual recognition memory, whether assessed with the visual paired-comparison (VPC) task (Bachevalier et al., 1993) or the delayed nonmatching-to-sample (DNMS) task (Málková et al., 1995). The present study demonstrates that despite their difficulty to recognize the trial-unique objects used for VPC and DNMS, infants with neonatal MTL removal retain the ability to distinguish objects that they have never encountered before from the highly familiar items that have been part of their daily environment since birth. This provides further evidence that early, like late MTL removal spare visual habit formation (Málková et al., 1995).

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