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AGE EFFECTS ON SOCIAL BEHAVIOR DEFICITS FOLLOWING PREFRONTAL LESIONS IN MONKEYS

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SUMMARY

Prolonged observation of rhesus monkey social behavior has shown no deficits among infants and yearlings which have undergone bilateral ablation of the prefrontal cortex. However, the behavioral deficits common to prefrontal lobectomy did appear with an increasing severity among 2- and 3-year-old juveniles and in adults. These deficits include decreased use of face and voice for communication, alterations in aggressiveness and patterns of grooming, decreased participation in play activity and frequent aimless hyperactivity.

It appears that a certain degree of maturation is required for the social effects of prefrontal lobectomy to be expressed. Rhesus infants operated on at 2 weeks, 5 months and 12 months of age show minimal, if any, deficits. Older juveniles and adults, however, do not maintain most behavioral patterns of social interaction. Harlow's results regarding deficits in intellectual development on learning performance tests are discussed. It is concluded that the appearance of social awareness and of intellectual maturity may occur at different times in a monkey's development.

INTRODUCTION

Prefrontal cortical lesions in monkeys produce alterations in performance on delayed response, delayed alternation and go–no go discrimination tasks[9]. However, changes in activity patterns and in social behavior have also been noted[2,6]. More specifically, monkeys with the prefrontal lobes amputated exhibit a decreased use of their face and voice in social communication, impoverishment of maternal behavior, and alterations in their aggressiveness and in their patterns of grooming[3]. Animals with major prefrontal lesions also fail to rejoin their social groups in a free-ranging situation[10].

TABLE I

GROUP COMPOSITION

Group number	*Animal*	*Sex*	*Year born*	*Animal*	*Sex*	*Year born*
1	107	M*	1955	I457	F	?**
	ZU	F	1964	inf	F	1969**
	Baby	M	1969	L4	M	1965
	A141	F	1968	LL	F	1961
2	KP	M*	1959	1N	F	1964
	NF	F	1961**	W5	F	1966
	BL	F	1969	UM	F	?
	YN	F	1963	um	F	?
	J4	F	1965	5U	M	1966
	FQ	F	1965	U9	M	1966
3	DP	M*	1958	NM	F	1961
	NI	F	1961**	Ba	F	1970**
	Bc	F	1970	IK	F	1960
	EL	F	1959	Be	F	1970
	Bb	F	1970	DC	F	1958
	HR	F	1959**	IFT	F	1969
	Inf	M	1969	W7	M	1966
	IR	F	1967			
4	EZ	M**	1959	OI	F	1964
	TY	F	1962*	S5	F	1966
	Bi2	F	1970	N1	M	1966
	GG	F	1964**	1M	M	1967
	NK	F	1961	U	M	1968
	Bd	F	1970	1G	F	1967
5	AG	M*	1958	YP	F	1963**
	GL	F	1964	B3	M	1965
	Bi1	M	1970**	1S	M	1967
	BX	F	1958	ZL	F	1964
	Bg	M	1970	Bh	F	1970
	3X	F	1967			

* Indicates dominant male of the group.
** Indicates monkey died or was sacrificed during the study.

Little is known concerning the effects of age at operation and changes in social behavior. Earlier studies have shown a sparing of performance deficit on the delayed response task, string test, and on discrimination learning following neonatal prefrontal lesions[1]. Animals under the age of two years have tended not to show social behavioral deficits following cerebral lesions[8]. Available evidence regarding functions outside the social sphere have generally indicated that lesions in the newborn or young animals are usually associated with preserved capacity.

The present study attempts to define the critical age at which social behavioral deficits begin to appear following prefrontal ablations. Infants, yearlings, and 2- and 3-year-old juvenile rhesus monkeys sustained bilateral removals of the prefrontal lobe.

Prolonged pre- and postoperative observations of their patterns of social behavior demonstrated minor or no deficits among the younger animals. However, the prefrontal social behavioral deficits did appear with an increasing severity among 2- and 3-year-old juveniles and in adults.

METHODS

Social groups

Five separate social groups of 6–12 animals each were utilized for the present study. The composition of these groups is seen from Table I. The groups were maintained in outdoor wire mesh enclosures (25 ft. × 8 ft. × 8 ft. each) in a semi-rural setting in Puerto Rico from September 1969 through September 1970. The monkeys were fed purina monkey pellets from food hoppers. Water was available *ad libitum*.

Observational methods

The groups were observed over a 13-month period. All monkeys received a minimum of 5 months of preoperative observation. Surgery was then performed on the available animals over the next 4 months. The final 4 months of the observational period was free from operative procedures. Each animal designated for surgery was watched intensively for a total of 12 min evenly distributed within each hour of observation. At the same time, group activities were noted throughout. Use of a checklist permitted a characterization of the proportion of time spent in the various categories of behavior. These categories included grooming, aggressive behavior, sexual behavior, play activity, general levels of activity, vocalizations, and dominance interactions. At the time of an animal's reintroduction into his group following surgery, a 45–70 min tape recording of all ensuing events was taken.

Operative procedures

The entire social group was food deprived for a 24-h period prior to the removal of a single animal for surgery. The designated animal was then shifted to the main laboratory and anesthetized with i.v. injections of pentobarbital (35 mg/kg). Following intubation, the animals were placed on the operative table, their heads sterily prepped and draped and a bilateral craniotomy was carried out. Subsequent to removal of cortical tissue by sucker aspiration, the bone flaps were replaced and the muscle and skin layers reapposed. Postoperatively, a single intramuscular injection of procain penicillin (200,000 units) was given. In addition, 60 ml physiological saline injections were given subcutaneously for hydration.

Table II depicts all animals operated in the present experiment and includes the dates of their operation and of their return to the social group. The extent of the lesion is illustrated in Fig. 1. The removals encompassed all cortical tissue lying anterior to the frontal eye fields and included the cortex of the orbitofrontal region. Lesion encroachment on the lateral olfactory tracts, the substantia innominata, and the anterior cingulate cortex was avoided in all instances. One 2-week-old infant died during the first 12 h following surgery. Another infant of a similar age (Bi2) was adopt-

TABLE II

PREFRONTAL OPERATE MONKEYS

Animal	*Group*	*Sex*	*Date of surgery*	*Date returned*
1S	3	M	Feb. 3, 1970	Mar. 2, 1970
1M	4	M	Feb. 10, 1970	Feb. 13, 1970
U	4	M	Apr. 22, 1970	Apr. 27, 1970
1FT	3	F	Apr. 28, 1970	Apr. 30, 1970
Bb	3	F	May 12, 1970	May 14, 1970
Bi2	5	F	May 28, 1970	June 1, 1970

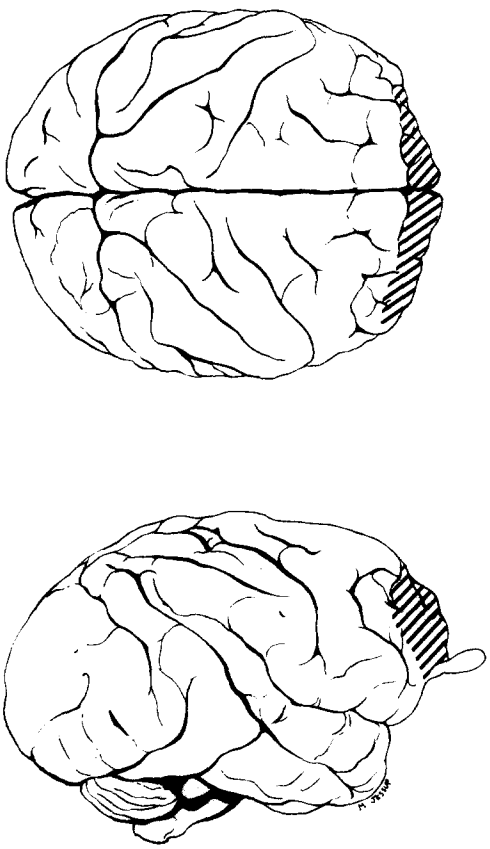

Fig. 1. Schema of prefrontal lesion extent of 5-month infant Bb.

ed by the dead infant's mother. After a few days of preoperative observation, the second infant underwent surgery. This infant was given a 10 ml blood transfusion and was returned to its adopted mother within 24 h.

All operates were held in the indoors animal quarters in single cages until fully recovered from anesthesia. Infants were returned to their mothers within 24 h. All animals were generally reintroduced to their social groups by the 5th postoperative

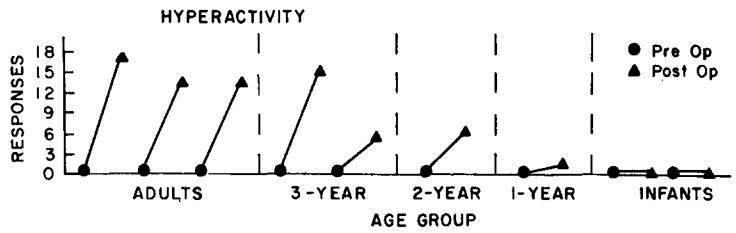

Fig. 2. Pre- and postoperative stereotypic behavior of prefrontal monkeys. The numbers refer to average responses for each hour of observation. Note the lack of postoperative hyperactive behavior in the 1-year and infant age group.

day. One male, 1S, developed a scalp infection which required treatment and he was not returned to his group for one month.

RESULTS

The *3-year-old animals* exhibited easily discernible changes in behavior similar to adult animals of another study[3]. Their food ingestion diminished immediately following surgery while they were still held in single cages. However, their weight loss was not severe and the animals soon regained their preoperative weights.

During the early period following their return, the 3-year-olds alternated periods of quiet and immobility with periods of greatly increased locomotor activity. They were hyperreactive to external stimuli. When approached by their peers, they grimaced, uttered brief screams and then entered bouts of locomotor activity. The approach of the observer or of caretakers also typically stimulated heightened locomotor activity. This hyperactive behavior declined through time, though it remained prominent in the juvenile's behavioral repertoire (see Fig. 2). All diagrams will compare the age effects with those of adult animals.

The aggressive behavior initiated by the 3-year-old operates dropped considerably as can be seen from Fig. 3. At the same time, aggressive displays directed towards the operates were generally high during the first weeks following surgery but decreased through time. Within a week following its reintroduction, 1M received a severe tail bite and was removed from the group for treatment. These aggressive encounters

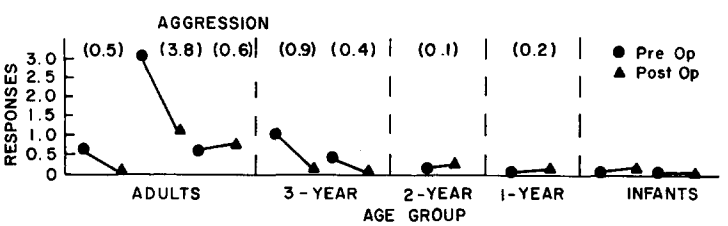

Fig. 3. Pre- and postoperative aggressive interactions initiated by prefrontal monkeys. The responses are averaged per hour observation. The numbers in parentheses represent responses given in the first 5 non-operative months, treated as control data. Note the definite drop in aggressive behavior of most adults and 3-year-old juveniles.

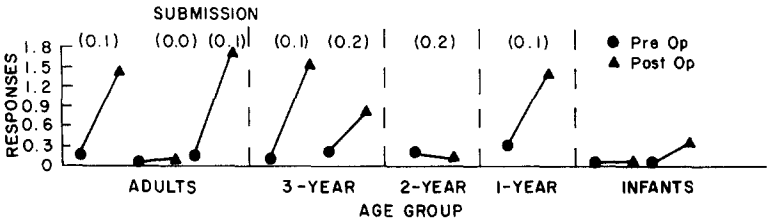

Fig. 4. Average responses per hour observation of submissive behavior of prefrontal monkeys. The numbers in parentheses are average responses during the 5-month control observations. Note the definite increase of submissive gestures in all age groups but infants and 2-year-olds. The one adult exception was the dominant female before surgery.

seemed precipitated by the inappropriateness of the operate's responses towards their group members.

As expected with the initial rise of antagonistic behavior directed against the operates, the latter exhibited increases in the frequency of submissive grimace and crouch responses as shown in Fig. 4. However, the frequency of this behavior also decreased through time.

Both 3-year-old males manifested a large reduction in the time spent grooming other group members (see Fig. 5). However, the time spent in self-grooming increased after surgery.

Fig. 6 shows the pre- and postoperative frequencies of play behavior of these operates. Adult play activity was not significant and hence is not included in the figure. Both 3-year-old males exhibited sharp decreases following surgery. During the first postoperative weeks, male 1M often remained seated in a slumped position while two other juveniles circled him playfully.

The 3-year-old operates showed nearly complete losses in vocal activity (see Fig. 7). The frequencies of screams and hoots remained the same for one male while the other decreased its scream frequency. Both lost completely responses in the grunt category.

The *2-year-old operated male* exhibited only a part of the social behavioral deficit of the prefrontal syndrome. In contrast to the 3-year-old operates, he maintained his body weight postoperatively. However, on reintroduction to his group, he

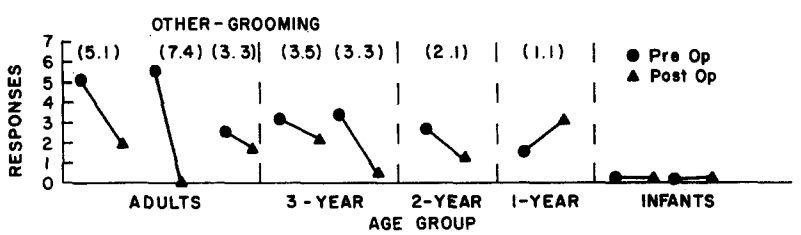

Fig. 5. Social grooming responses per hour observation performed by prefrontal monkeys. The numbers in parentheses refer to control observations. Note the definite drop in other-grooming by all age groups except yearlings and infants and the close correspondence of control to preoperative behavior.

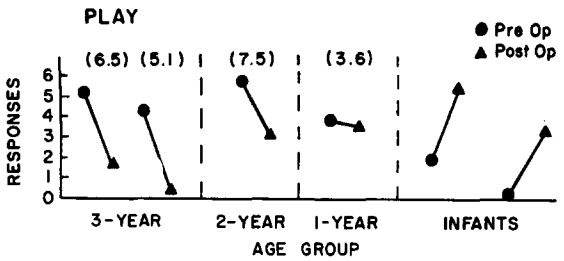

Fig. 6. Average responses per hour observation of play activity engaged in by juvenile prefrontal monkeys. The numbers in parentheses refer to control data. Note the abrupt decrease of play behavior among the 3- and 2-year-olds, the relative stability of the yearlings and the sharp increase among the infants.

remained extremely hypoactive for about a week. Then he began to exhibit bouts of pacing activity though these decreased in frequency through time (see Fig. 2). This 2-year-old also showed an initial hyperreactivity similar to that of the 3-year-olds. This included grimacing and slapping the air jerkily with his hands at the approach of other juveniles. This behavior ceased within a few weeks.

In contrast to the 3-year-old operates, the aggressive behavior initiated by the 2-year-old remained at about the same level after surgery as before (see Fig. 3). Similarly, the frequency of submissive responses remained unchanged after the first post-operative weeks (see Fig. 4).

Contrary to expectations and to the behavior of the other juvenile operates, the grooming activities of the 2-year-old male decreased by about 50% following surgery as revealed in Fig. 5. This decrease affected self- as well as other-grooming. Play behavior also showed nearly a 50% drop (Fig. 6). Subsequently, however, the 2-year-old operate spent time trying to initiate play with 3-year-old operate 1M.

The 2-year-old operate showed a decrease in vocalization frequency comparable to that of the 3-year-old prefrontal operates (see Fig. 7). He completely dispensed with geckering but maintained some vocal activity in other categories.

In contrast to the 2- and 3-year-old juveniles, the *yearling* following surgery showed only traces of the prefrontal syndrome. There was no weight loss following surgery. On reintroduction to the social group, the operated yearling female was retrieved and otherwise normally treated by her mother. Though the yearling showed

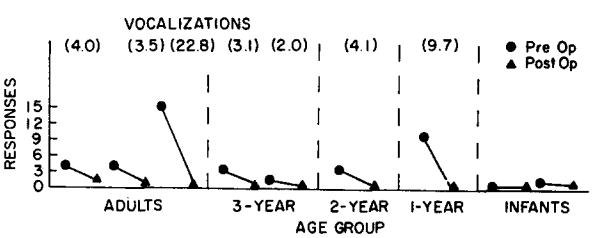

Fig. 7. Total vocal activity of prefrontal monkeys averaged per hour observation. The numbers in parentheses represent control data. There is a near absence of vocal behavior for all age groups post-operatively, with the infants remaining stable.

an initial tendency towards hypomotility interspersed with bouts of pacing (see Fig. 2), this ceased within the first week and a half. The yearling never showed any indication of hyperreactivity to threatening stimuli.

Following surgery the yearling exhibited no change in the frequency of its aggressive interactions with other animals (Fig. 3). In these instances all facial expressions and gestures appeared normal. Contrary to the expected result, the yearling nearly quintupled her frequency of submissive responding. This increase in grimace behavior reflects increased submissive responses emitted to other group members not previously grimaced to (*i.e.*, new infants).

Grooming interactions initiated by the yearling showed nearly a 100% increase (Fig. 5). This change reflected increases both in self- and in other-grooming. Play behavior, as shown in Fig. 6, remained unchanged.

The yearling's vocal activity decreased following surgery as revealed in Fig. 7. The grunt category was completely abolished while the other 3 categories (hoot, scream, and gecker) were still utilized but to a lesser extent.

The *5-month-* and the *2-week-old infants* were unchanged by the prefrontal operations. Both were alert, investigative and showed no motor impairments. When restored to their mothers, both clung and attached themselves to the nipple without hesitation. Upon reintroduction to the group both showed normal social reactions: they approached peers for play (Bb) and showed curiosity towards others (Bi2) and towards the environment. They showed no signs of pacing hyperactivity or of hyperreactive responses to outside stimuli as can be seen from Fig. 2. Both showed slight increases in the aggressive interactions (see Fig. 3) while their grimace frequencies remained unchanged (see Fig. 4). The slight increase in submissive responses of the 2-week-old infant likely reflects a dominance shift taking place among the adult females of her group.

Both infants remained unchanged with respect to grooming frequencies as shown in Fig. 5. As expected, the play behavior of both increased as they grew older (see Fig. 6). Vocal responses by the 5-month-old remained unchanged, a slight decrease affecting only the screams. The vocal activity of the 2-week-old infant changed, hoots and screams appearing for the first time following surgery (see Fig. 7).

The overall social behavior of the two infants appeared normal in all respects. However, at the time of sacrifice, all infants were removed from their mothers and individually caged. The normal infants became withdrawn, refused food, and eventually died while operated infants remained alert and curious, threatened humans, and even ate pieces of fruit prior to their sacrifice.

DISCUSSION

The 3-year-old prefrontally operated juveniles exhibited definite behavioral deficits. These deficits resemble the alterations observed among adult rhesus monkeys subjected to the same removal. The alterations produced include an increased stereotyped locomotor activity (pacing), reduced aggressiveness, a higher frequency of submissive gestures, and a reduced vocal activity. Alterations in grooming patterns

were also similar in that, following surgery, most grooming was self-grooming.

The 2-year-old operate also exhibited many of the behavioral deficits characteristic of the 3-year-old and adult operates. There were definite increases in stereotyped pacing activity, decreases in other-grooming, reduced vocal activity, and diminished play behavior. However, the prefrontal operation in the 2-year-old failed to alter aggressive and submissive interactions.

The yearling showed even fewer indications of changed social behavior. It exhibited some stereotypic pacing behavior but only for the first 1.5 weeks after surgery. The aggressive displays and grooming behaviors showed increases while play behavior remained stable. However, vocal activity decreased while submissive responses increased — both to a considerable extent.

The infants remained essentially stable in all behavioral categories except play, where a great increase ultimately was seen. Thus, the changes observed following surgery in this age group appeared more in the way of maturational changes than as a consequence of the surgery.

The present study suggests the critical age for the appearance of hyperactivity and stereotyped pacing activity following bilateral prefrontal lesions is at about 24 months. This finding agrees with Tucker and Kling[11] who described the appearance of hyperactivity at the age of 2 years in a monkey prefrontally operated in infancy. Their infants which underwent prefrontal removals during the newborn period exhibited no behavioral abnormalities during their first postoperative year in agreement with the present findings.

Harlow *et al.*[4] studied performance of rhesus monkeys prefrontally operated at 5 days, 5 months, and 2 years of age. They also observed no changes in the two youngest groups and hyperactivity and compulsive pacing during training-cage testing of the 2-year-olds. An aspect of the hyperactivity and forced pacing of prefrontal operates which has not received attention is that it appears alternately with periods of abnormal quietness and immobility. A normal monkey whether ambulating or sitting is actively engaged, nonetheless, in doing something, *i.e.*, he scans the environment, he grooms himself or others, he investigates objects, he eats, etc. In contrast to this, the 3-year-old and adult prefrontal operates spend much of their time just sitting and staring into space. They show a minimal curiosity or interest in any part of their surroundings. The 2-year-old operate also exhibited episodes of abrupt and near-total stillness but this behavior began to disappear after the first month. Neither the yearling (after the first postoperative week) nor the infants displayed any such abnormal immobile behavior.

Kling and Tucker[8] found that maternal rearing is possible after prefrontal cortical lesions. The present study confirms this for groups kept in large enclosures. Kling and Tucker also concluded that ablations of the dorsolateral frontal cortex in the newborn monkey result in sparing of effect on a delayed response task through the first year of life. However, they found indications that this sparing effect may begin to diminish between 18–24 months of age. In contrast to this report, Harlow *et al.*[5] report deficits in learning performance (delayed response, object discrimination, oddity learning set) at 5 months as well as at 12 and 24 months of age. However,

infants operated on at 5 days of age did not show such deficits.

Kling and Green[7] did not find any behavioral changes in newborn infants undergoing amygdala ablation during the first year of life. They concluded that a certain degree of sexual maturation is required for the expression of the effects of amygdalectomy. The present study also indicates that significant social maturation must be present for the adverse effects of prefrontal lobectomy to be felt. The continued maintenance of social bonds by the operated infants and yearlings and the loss of such behavior in the 2- and 3-year-old operates reflects the importance of time in the socialization of rhesus monkeys. Intellectual development with regards to learning and perception seems to mature at a faster rate than does the ability to communicate properly. Hence, Harlow's results complement this study in aiding our understanding of brain development in its many manifestations.

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