Perinatal injuries to extravisual cortex enhance the significance of visual cortex for performance of a visual habit

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It has been established that if rats are prepared with perinatal injuries to the visual neocortex, are trained as adults on the black-white discrimination, and are then prepared with second-stage ablations of the rest of the neocortex, the effects of the second-stage injuries upon performance of the task are much more severe than those that are produced by extravisual injuries if the first-stage injuries to the visual neocortex are also inflicted in adulthood. This investigation presents a symmetrical result, that is, an enhancement of the deficits produced by injuries to the visual neocortex in adulthood by preexisting perinatal injuries to the extravisual cortex.

Horel, Bettinger, Royce, and Meyer (1966) compared the effects of bilateral ablations of the anterior cortex upon the performances of rats that had learned a black-white discrimination problem while their brains were intact with those of rats that had learned the same problem after having been prepared with first-stage bilateral ablations of the posterior cortex. The findings were that even though the latter animals were tested for retention after second-stage injuries that completed the destruction of the cortex, the two groups of subjects relearned the problem at the same rate. Hence, it appeared that, insofar as performance of a simple visual habit is concerned, the cost of an injury to the extravisual cortex is completely independent of whether or not the visual neocortex is intact.

Howarth, Meyer, and Meyer (1979) have recently confirmed the foregoing set of observations. But Howarth et al. also studied the effects of perinatal injuries to the posterior cortex upon the consequences for performance of the problem of anterior injuries in adulthood. They found that, for those conditions, second-stage bilateral ablations of the anterior cortex severely attenuate the rate at which the problem is relearned. Indeed, their best estimate was that the latter subjects required as many trials to relearn the problem as would have been expected if the rats had been prepared with one-stage bilateral ablations of the entire neocortex.

In this investigation, we have asked the converse question, namely, whether perinatal anterior injuries will bring about a comparable enhancement of the

role of systems related to the posterior cortex in performance of the black-white problem. It is thoroughly established that posterior subjects have greater impairments of performance of the problem than animals with anterior injuries, and also that the rate at which they relearn the problem is the same as the rate at which the problem is learned by naive posterior preparations (cf. Meyer & Meyer, 1977, for review). Moreover, Horel et al. (1966) have observed that the rate at which posterior subjects relearn the problem is completely independent of whether or not the rats learn the problem as normal animals or after having been prepared with first-stage ablations of the anterior cortex in adulthood.

While the study was in progress, we encountered an important methodological problem. For some unknown reason, the rats employed in this investigation were faster learners than the rats that were used in the study of Howarth et al. (1979). That raised the question of whether we could safely compare the postoperative learning scores of the subjects of the two experiments. Therefore, we were prompted to replicate a finding of Howarth et al. with respect to the effects of adult anterior injuries upon the rate at which the black-white problem is relearned as a means of assessing the extent to which our findings were affected by differences in methods and/or strains of animals.

We also examined the impairments of performance that result if rats are trained on the problem prior to surgery but are not retrained until after their second-stage ablations. We expected the animals to have severe impairments of postoperative retention of the problem, because a "serial effect" had not been obtained with the black-white task in any experiments except those in which the animals were trained on the task before the first operation and then

This research was supported by Grant MH06211 from the National Institute of Mental Health, and was conducted while the second, third, and fourth authors were Fellow in Developmental Psychobiology with support from Training Grant MH15677 from the National Institute of Mental Health.

retrained on the task between the two operations (cf. Finger, 1978; Kircher, Braun, Meyer, & Meyer, 1970; Meyer & Meyer, in press; Petrino & Carew, 1969; Thompson, 1960). Therefore, we included a group in the study to provide a measure of the maximal effect upon postoperative performance of the black-white problem that might be expected after an injury to the entire neocortex.

METHODS

Subjects and Design

The subjects were 144 male Long-Evans hooded rats. The animals of Groups 7A-102P, 63A-102P, and 63C-102P were born in the laboratory's breeding colony. Groups 102A and 102A-113P were a mixture of rats from the breeding colony and a commercial supplier, Blue Spruce Farms. The litters of rats that were raised in the colony were culled to a maximum of nine pups when they were 7 days old, were weaned when they were 21-25 days old, and then were housed in groups until they were 63 days old.

The Ns and treatments for each of the groups are given in Figure 1. The groups are designated by combinations of numbers (7, 63, 102, and 113), which refer to the ages of the subjects at the time a given treatment was performed, and of letters, which refer to the types of treatments inflicted (C for control incisions, A for anterior ablations, and P for posterior ablations). Thus, the first group, 7A-102P, was prepared with first-stage anterior ablations when the animals were 7 days old, and then with second-stage posterior ablations when the animals were 102 days old. The diagrams depict the status of the cortex following each of the procedures, and describe new injuries to the cortex in black and older injuries with crosshatched lines. The subjects of all groups were first trained on the black-white problem (OL) when they were 100 days old. Tests for retention (RL) for most groups occurred when the animals were 113 days old. However, retraining for Group 102A-113P was delayed until the subjects were 124 days old so that those animals would have the same recovery time from their second-stage posterior ablations as the other adult preparations.

Surgical Procedures

The neonatal surgeries were performed while the pups were anesthetized with Metofane. First, the animal was taped into a form-fitting clay mold. The scalp was then excised, and the calvarium anterior to bregma was removed with fine iris scissors. A 1-mm strip of the calvarium was left intact above the sagittal sinus. Thereafter, the meninges of the anterior cortex were carefully removed through the use of cotton swabs and fine forceps.

When the ablations were completed, the scalp was sutured and the pup's ear was marked by clipping. The animal was then returned to the care of its mother.

The surgical procedures for the injuries inflicted in adulthood were carried out while the animals were anesthetized with sodium pentobarbital. The posterior ablations were intended to include all of the cortex from bregma to the occipital pole and from the sagittal sinus to the rhinal sulci. The lesions typically consisted of bilateral destruction of areas 7, 17, 18, 18A, and 20, as defined by Krieg (1946). The lesions thus involved all the areas of the cortex that are known to receive projections from the dorsal lateral geniculate nuclei and/or the nuclei lateralis posterior thalami (Hughes, 1977). The bilateral anterior injuries were intended to include all the dorsolateral cortex that lies anterior to bregma and between the sagittal sinus and the rhinal sulci. As in the perinatal surgeries, thin strips of bone were left intact along the midline of the calvarium. In both of the procedures, the cortex was destroyed by the pia-stripping method of Woolsey (cf. Meyer & Meyer, 1971), and the animals were given a broad-band antibiotic when the surgeries were completed.

As Horel et al. (1966) first observed, and the recent experiments of Braun (1975) have confirmed, injuries to the anterior cortex which involve the tissues adjacent to the rhinal sulci always bring about aphagias. In this investigation, the effect was noted in Groups 102A and 102A-113P, and therefore those animals were fed a sweetened wet mash until, after several days, they once again would eat dry pellets.

Behavioral Procedures

The subjects were trained on the black-white problem in a version of the Thompson-Bryant (1955) modification of the Yerkes-Watson-Munn apparatus. It consisted of a startbox, a choice compartment, and a goalbox. The task of the subject was to exit from the startbox when the trainer raised a guillotine door, and then from the choice compartment into the goalbox by knocking down an unlocked white door in a partition between the choice compartment and the goalbox. The white door was paired with a locked black door, and their left-right positions were changed from trial to trial in accordance with a Gellermann (1933) series. The partition that held the doors was black, as were the walls of the startbox, goalbox, and choice compartment. The apparatus was illuminated by small fluorescent lamps in fixtures that were mounted on the apparatus' transparent lid, and hence the arrangement provided the trainer with a one-way view of the proceedings.

The subjects' incentive for performance of the task was avoidance of very mild shocks to the feet from a grid that formed the floors of the startbox and the choice compartment. The avoidance reactions were established through pretraining that began when the subjects were 98 days old. By that time, the subjects had been handled every day for 5 days. They then were permitted to explore the apparatus on Day 98 for a period of 15 min. On Day 99, they were shaped with mild footshocks to exit quickly from the startbox, and then to exit from the choice compartment by knocking down either one of two "neutral" doors which displayed arrays of black and white stripes. The habits thus established are extremely persistent after injuries to the dorsolateral cortex (cf. Meyer & Meyer, 1977), and therefore the subjects were pretrained before training (OL) but not before their tests for retention (RL).

Histological Procedures

When the behavioral procedures were completed, the subjects were given a lethal dose of sodium pentobarbital and then perfused with saline followed by 10% Formalin. Their brains were removed and Lashley diagrams were drawn of the extents of the injuries to the cortex. Also, the extents of the cortical ablations for all the groups were ranked by several judges, and Spearman rho correlation coefficients were computed for the rankings thus obtained and the animals' relearning scores.

Group	n	7	63	100	102	113	124
7A-102P	36			OL		RL	
63A-102P	33			OL		RL	
63C-102P	36			OL		RL	
102A	21			OL		RL	
102A-113P	18			OL			RL

Figure 1. Summary of the treatments of the groups, and the times of the treatments. OL refers to original learning of the task, and RL to relearning of the task. Preexisting injuries shown in crosshatch.

RESULTS

Figures 2, 3, 4, 5, and 6 present the results of the histological analyses, and also the individual OL and RL scores of subjects. There were no apparent inter-group differences between the scopes of the ablations of the animals in Groups 7A-102P, 63A-102P, and

102A-113P. The posterior injuries of the subjects of Group 63C-102P were comparable to those of the many other radical posterior preparations whose behaviors have been studied in our laboratory (cf. Meyer & Meyer, 1977). The anterior injuries of the subjects of Group 102A were comparable to those of the anterior subjects of the Horel et al. (1966) investi-

Figure 2. OL scores, RL scores, and extents of injuries for Group 7A-102P.

Figure 4. OL scores, RL scores, and extents of injuries for Group 63C-102P.

Figure 3. OL scores, RL scores, and extents of injuries for Group 63A-102P.

Figure 5. OL scores, RL scores, and extents of injuries for Group 102A.

Figure 6. OL scores, RL scores, and extents of injuries for Group 102A-113P.

gation. The intragroup correlations between the scores of the ablations and the relearning scores were .14, .16, .21, .08, and .01 for Groups 7A-102P, 63A-102P, 63C-102P, 102A, and 102A-113P, respectively. None of the correlations was significant beyond the .05 level.

Table 1 presents the mean trials and errors, and the standard errors of the means of those scores, for original learning (OL) and relearning (RL) for the various groups of subjects. The groups that were normal or else had sustained a control operation prior to OL (Groups 63C-102P, 102A, and 102A-113P) required about 18 to 19 trials to learn the problem and committed about 11 errors. The 7A-102P subjects, which at the time had been recovering from their perinatal injuries for 93 days, also learned the problem at about the same rate and with scores of 20 trials and 12 errors. The 63A-102P subjects required about 25 trials to learn the problem and committed 15 errors, but neither of the scores was significantly higher than the comparable scores of the 7A-102P preparations.

The relearning scores present an altogether different picture. Thus, the subjects of both Group 63A-102P

and Group 63C-102P relearned the problem in about 20 trials and committed about 12 errors. However, the subjects of Group 7A-102P required about 31 trials and committed about 18 errors. Also, their trials score was only slightly lower than the trials score for the subjects of Group 102A-113P, which had received no training between their operations and hence were expected to be as retarded as animals prepared with one-stage ablations of the entire dorso-lateral cortex. The error scores for the latter two groups proved to be exactly the same, and in both instances the scores were about 6 errors higher than the average of about 12 errors for Groups 63A-102P and 63C-102P. The trial scores for relearning of the problem by Groups 7A-102P and 63A-102P were different at the .06 level ($t = 1.91$), and their error scores were significantly different beyond the .05 level ($t = 2.1$).

DISCUSSION

First, we shall discuss our concern about the fact that, in this study, the OL scores for the subjects that were trained prior to surgery were low. For about 20 years, such scores have been employed in our program as a means of assessing the comparabilities of findings obtained by many different people and with several different strains of hooded rats. At this stage, we know, from experiments conducted with approximately 2,000 subjects, that under our conditions the expected value for an OL score is either approximately 50 massed, or 25 spaced, training trials. Hence, although our current OL scores for unoperated subjects or control subjects were 18-19 trials, and therefore were deviant from our customary values by only 6-7 spaced trials, it was clear that the RL scores of the groups would need to be interpreted with caution.

About 10 years ago, a similar problem was encountered by Jonason, Lauber, Robbins, Meyer, and Meyer (1970). In their investigation, posterior subjects with unusually low preoperative scores (about 37 massed training trials, or the equivalent of 18.5 spaced training trials), relearned the problem in approximately 41 massed trials. The latter number corresponds to 20.5 spaced trials, which, in the present study, was the RL score for Group 63C-102P. The fact that the latter score was 3 or 4 trials lower than the characteristic RL score for posterior subjects that are trained by the spaced-trial procedure (Glendenning, 1972) led us to ask if we could replicate the 102A result of Howarth et al. (1979) (their Group 63C). We found that even though the OL scores of the subjects were 28.6 spaced training trials (Howarth et al.) and 19.3 spaced training trials (present study), the RL scores for the two groups were 17.6 and 17.1 mean spaced trials, respectively. Hence, although we still are somewhat bothered by the fact that our OL scores for unoperated animals were low,

Table 1
Mean Scores to Criterion

	Original Learning				Relearning			
	Trials		Errors		Trials		Errors	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE
7A-102P	20.3	2.2	12.2	1.2	30.9	4.9	17.9	2.8
63A-102P	25.3	2.4	15.0	1.2	19.9	2.8	11.4	1.3
63C-102P	17.8	1.7	11.2	1.0	20.5	2.9	12.6	1.6
102A	19.3	2.7	11.5	1.3	17.1	2.4	12.1	1.3
102A-113P	18.7	1.8	10.6	.8	34.4	4.8	17.9	2.0

we concur in the conclusion of Jonason et al. (1970) that RL scores are only marginally affected by procedural variations which result in large changes in the values of OL scores.

Our findings with respect to Groups 63C-102P and 63A-102P were exactly as predicted from comparable outcomes of the Horel et al. (1966) investigation. Thus, the effects of second-stage bilateral ablations of the visual neocortex are completely independent of whether or not the subjects have previously sustained extravisual anterior injuries provided that the animals with prior anterior injuries in adulthood are given interoperative training on the problem. If the training is omitted, as is shown by the findings for Group 102A-113P, the second-stage bilateral posterior injuries bring about severe impairments of relearning of the problem.

As we had expected, the deficits exhibited by Group 102A-113P proved to be approximately the same as the impairments of subjects that are retrained on the problem after having been prepared with one-stage bilateral ablations of the entire dorsolateral cortex. Thus, such subjects will relearn the problem in about 74 massed trials (Meyer, Yutzey, Dalby, & Meyer, 1968), and hence would be predicted, from Glendenning's (1972) rule (i.e., massed trials/2 = spaced trials), to relearn the problem in approximately 37 spaced trials. The fact that it took Group 102A-113P 34 spaced trials to relearn the problem is thus another confirmation of the rule's validity, which has also been supported by previous observations of Glendenning (1972) and Howarth et al. (1979).

In the Howarth et al. (1979) experiment, a group which we would term 7P-102A (their Group 7P) relearned the problem in 34.5 spaced trials. The animals also committed 17.1 ± 2.5 errors. Their mean trials and errors were thus within one trial and one error of the mean trials and errors of our Group 102A-113P. Moreover, although our Group 7A-102P relearned the problem in several fewer trials than the 7P-102A subjects of the Howarth et al. investigation, there were almost no differences between the error scores of the latter preparations and those of our Groups 7A-102P and 102A-113P (rounded scores 17 ± 3 , 18 ± 3 , and 18 ± 2 , respectively). Hence, we conclude that a perinatal injury to either the visual or the extravisual cortex induces a reorganization of the functions of the still-remaining cortical systems such that, if those systems are subsequently destroyed, the effects upon retention of the black-white problem are in either instance about as severe as the effects of complete bilateral ablations of the dorsolateral cortex in adulthood.

Cunningham, Huddleston, and Murray (1979) have observed that perinatal injuries to the posterior cortex will bring about a number of important alter-

ations of the structure of the rat's central visual mechanism. Howarth et al. (1979), whose paper was in press at the time the foregoing findings were reported, had suggested that their own observations had indicated that studies of that kind were likely to be very fruitful. We now strongly agree, because the results of this experiment have shown that the effect described by Howarth et al. can be produced by perinatal injuries to either the visual or the extravisual cortex. Hence, if we suppose that the inductions are relatable to changes in the visual mechanism, which is not unreasonable in view of the fact that the animals were tested for performance of a simple visual problem, they will have to be changes that are not explicitly produced by early posterior injuries.

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(Received for publication September 6, 1979;
revision accepted February 20, 1980.)