

of lever pressing from the first three test sessions to the last three ($p < .005$). In addition, the animals with lateral frontal lesions showed reliably smaller increases in rate of lever pressing than did the normal animals ($p < .0005$). The effect of repeated presentation of the stimuli within test sessions was not significant. Furthermore, there were no reliable group differences in the number of lever presses in pre-stimulus periods.

The finding that the animals with frontal lesions were abnormally slow in increasing their rates of lever pressing, over successive stimulus periods, suggests that their ability to habituate responses to the novel stimuli was impaired. Furthermore, it appears that in the monkeys with orbital frontal lesions habituation occurred more slowly than it did in those with lateral frontal lesions. This interpretation is consistent with the view that orbital frontal ablation disturbs the animal's ability to suppress strong response tendencies more than lateral frontal ablation does.

On the other hand, these results appear to be equally consistent with the view that the animals with orbital frontal lesions had *less* difficulty than the other animals in suppressing another strong response tendency—the tendency to press the lever for food rewards. This view, however, is not supported by the finding that monkeys with orbital frontal ablations, trained to press a lever for food, show perseveration of these responses in extinction (2).

Indeed, on the basis of that finding one might have expected the monkeys with orbital frontal lesions not to suppress lever pressing when the novel stimuli were presented. It may be possible to resolve the apparent contradiction between these results and the present findings in the following manner. While monkeys with orbital frontal lesions show perseveration of food-rewarded responses in extinction, the responses of such monkeys to the initial presentation of the novel stimuli used in this study were strong enough to interfere with lever pressing and become dominant. This assumption that responses to the novel stimuli were initially dominant is supported by the finding that the lever-pressing rates of all animals dropped almost to zero when these stimuli were presented for the first time. According to the view that frontal lesions impair the ability to suppress the dominant response (3),

one might expect perseveration of responses to novel stimuli in these animals. In order to determine whether this analysis is valid, responses to novel stimuli as well as responses rewarded with food would have to be directly measured in monkeys with frontal lesions.

Although responses to the novel stimuli were not directly measured, it should be noted that orienting responses typically shown by monkeys in novel situations were observed in the animals during stimulus periods. However, one cannot rule out the possibility that the novel stimuli produced other kinds of responses, such as fear, which might have interrupted lever pressing.

Finally, it should be noted that lesions of the amygdala produce alterations in behavior which resemble those found in monkeys with orbital frontal lesions. Thus, amygdalotomized monkeys show enhancement of food-rewarded responses in extinction (5) and abnormally slow habituation of locomotor activity in the presence of novel stimuli (6). Moreover, since a portion

of the orbital frontal cortex and the amygdala are closely related anatomically (7), it appears that a direct comparison of the effects of lesions in these two areas on extinction and habituation would be fruitful.

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8. This experiment was performed during the tenure of a U.S. Public Health Service postdoctoral fellowship, MF-9588-C1, at the National Institute of Mental Health in the Section on Neuropsychology. I thank Drs. H. Enger Rosvold and Mortimer Mishkin for providing the facilities for performing this experiment, Morris Waxler for testing the animals, and Nathaniel Ehrlich for performing the statistical analyses.

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Newborn Attention as Affected by Medication during Labor

Abstract. *Babies, 2- to 4-days old, whose mothers received heavy medication during labor were less attentive than those babies whose mothers received light medication.*

Moya and Thorndike (1) have recently presented a comprehensive review of the effects of drugs used in labor on the fetus and newborn. The accumulation of data from experimental animal studies and human clinical investigations indicates that "The newborn shows marked susceptibility to the depressant effects of drugs used in labor. This heightened sensitivity is related in part to increased permeability of the blood-brain barrier, inefficient metabolism, and asphyxia and physical trauma associated with the delivery process." One of the important limitations of the human studies cited is that the evaluation of the neonate has been limited to what can be observed in the delivery room.

While there is good reason to expect that for the newborn the effect will persist beyond the immediate delivery, and will indeed persist beyond the normal adult period of pharmacological effectiveness (2), clearcut demonstration has been lacking largely because of the difficulty of finding sufficiently sensitive

techniques for evaluating the functioning of a baby who is a few days old. Standard neurological techniques are gross, and discriminate only marked pathology.

By means of a stimulus presentation technique similar to that of Fantz (3), a visual fixation on a series of three different stimuli has been used here to test the effect of medication during labor on visual attentiveness in the neonate.

Twenty full term babies from 2 to 4 days old, from normal deliveries and with no gross pathology constituted the study sample. Earlier than 2 days, eyelid swelling from silver nitrate administered at delivery impairs testing of vision. Three stimuli were presented in random order, each for a duration of 1 minute. Each experimental session contained three replications of the stimulus presentation, each with a new random ordering. Thus, there was a total of 9 minutes of stimulus exposure for each baby. All subjects were quietly awake at the start of a session. Three

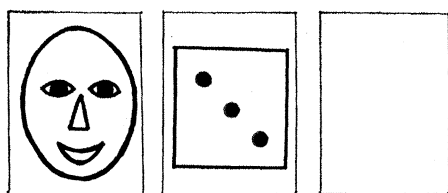


Fig. 1. Visual stimuli from left to right, face, die, blank.

additional babies were discontinued when they became distressed soon after the start of the test.

The stimuli as shown in Fig. 1 were drawn on sheets of paper (24×27.5 cm), except the blank stimulus, which was the same size paper with no drawing on it, were held in a frame about 20 to 25 cm from the baby's face in a direct line with his tonic neck reflex. The translucent stimuli were lit from behind so that 130 to 180 lu/m² of light fell on the baby's face. The observer was directly adjacent to the stimulus but not visible to the baby. The baby, remaining in his nursery crib, was completely unrestrained so that all behaviors were possible, including gross head turning and looking distinctly away from the stimulus.

Total time spent staring at, or scanning the stimulus area was contrasted with the total of the range of non-attentive behaviors, such as looking away, closing eyes, or fussing.

The range in individual differences in total looking time was from 93 to 426 seconds; mean, 235 seconds; S.D. = 97.1.

In seeking to establish a relationship between the medications administered to the mothers during their labor period and the total looking time of their respective infants, the investigators did not have information on the medication at the time of the visual testing, and therefore were not biased in their evaluation of the attentiveness of a baby.

The major drugs studied were meperidine, alphaprodine, pentobarbital, and promethazine. All are depressants and act in the same direction, although

not on the same centers of the central nervous system. The first three of this group act relatively rapidly, with peak times of less than 1½ hours.

Two analyses have been performed. The first is simply a division of the mothers into two groups, one of which had a depressant drug within 1½ hours of the delivery, and the other group had no drug in that period. The mean of total looking time for the group having had the drug within 1½ hours was 195 seconds ($N = 9$), while for the other group the mean was 287 seconds ($N = 11$); ($t = 2.32$, 17_{df} , $p < .025$).

The second analysis is more complicated in that total dosage of all drugs is included and is weighted for both size of dose and time of administration. For each administration of each drug a score of + or ++ was assigned. The single + represents a normal therapeutic dose of the particular drug in question, and ++ represents an above normal dosage of that drug. Meperidine, 75 to 100 mg, was +; 150 to 175 mg was ++; pentobarbital, 100 to 175 mg was +, 200 to 300 mg was ++; alphaprodine, 15 to 30 mg was +; promethazine, 25 to 50 mg was +, 75 to 100 mg was ++ (4). The factor of time was then weighted as follows: within 1½ hours before delivery, 4×; 1½ to 4 hours, 3×; 4 to 8 hours, 2×; more than 8 hours, 1×. Dosages for each drug were multiplied by the appropriate time factors and then summed for each subject.

The distribution of total looking times for each infant classified under the time-weighted dosage levels of his mother is shown in Table 1.

Pearson r for this distribution is $-.55$ ($p < .01$), indicating a significant negative correlation between time-weighted total dosage and total looking time; this means that the more drugs administered closer to delivery the less attentive is the infant likely to be.

Thus, both methods of analysis indicate that there is a significant relationship between the administration of certain drugs used in labor and the

attentiveness of the infants in this experimental situation. Normal clinical use of multiple drug combinations precludes analysis of the effects of a single drug.

Control on other variables indicated that individual differences in total looking time for all stimuli were, in the present sample, not related to sex of the infant, to birth weight, to length of labor, to gestational age (all were full term, normal infants), or to age (between 2 and 4½ days).

The stimuli themselves have a marked effect on the duration of visual attentiveness which they elicit. Out of the 180 seconds of exposure for each stimulus, the average attention toward the face is 105 seconds, while for the die and blank forms the averages are 88 and 42 seconds, respectively. All differences are significant ($p < .01$). These findings support Fantz's conclusion of stimulus discrimination by the neonate (3). No conclusion regarding perception of pattern is implied, since differences in stimulus complexity alone would suffice to explain the current results. The infant need merely orient longer toward sources of greater retinal stimulation in order that these findings be produced. (An average scan across the face stimulus encounters 4.0 white to black intersections, while for the die the average is 2.7, and for the blank, 0.) There was, however, no demonstration of a differential effect of drug administration upon greater or lesser discrimination of stimuli.

The demonstration of an effect on attention in the newborn of drugs used in labor has implications both for the understanding of drug actions and for visual attentiveness itself.

In the search for a stable yet sensitive measure of the quality of the organization of a newborn's behavior, it is encouraging to find that something centrally mediated and as delicate and fleeting as states of alert attentiveness can be found to be related to a significant independent variable, in this case, drugs used during labor.

On the basis of the limited, cross-sectional data, no shift in patterns of attention was found as between 2 and 4 days of age. A central question which remains unanswered is the persistence of the effect beyond the age of 4 days. Nevertheless, there is confirmation that some drug influence persists in the neonate for considerably longer than would be expected based on adult re-

Table 1. The total looking time (in seconds) is shown for a group of 19 babies. The dose-levels (all drugs) are time-weighted.

0*	Weighted drug dose						
	3	6	7	8	12	15	20
146	343	306	162	168	176	111	118
219	344	335		177	267		
297				181	293		
426				383			

* No drug given

actions to the same drugs in normal clinical doses, supporting the concept of greater vulnerability in the immature organism.

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4. The maximum dose for any depressant drug received by any single mother over the entire course of the labor was as follows: Meperidine, 175 mg; pentobarbital, 300 mg; alpha-prodine, 35 mg; promethazine, 125 mg. Delivery anesthesia is not a relevant consideration in this study, since only spinal anesthesia, if any, was used.

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Temperature Changes in the Rat in Response to Feeding

Abstract. *Feeding activity in fasted rats resulted in an immediate increase in brain temperature and a decrease in rectal temperature. The temperature changes did not correlate with any specific property of the food nor with the amount eaten. The responses were judged to be the result of reflex vasomotor changes resulting in widespread shifts in the direction of blood flow. They were not related to the regulation of food intake.*

The demonstration of hyperphagia and obesity in rats with bilateral lesions in the ventromedial nuclei of the hypothalamus, and starvation in rats with lesions lateral to these nuclei has focused attention on these regions of the brain as the basic central regulators of food intake (1). It has been inferred from the experimental evidence that activation of the ventromedial nuclei by some factor or factors related to the replenishment of nutrients normally brings about satiety through inhibition of feeding behavior mediated through structures in the lateral regions of the hypothalamus. The factor or factors responsible for activation of the ventromedial nuclei have not yet been identified. Several hypotheses have been proposed and numerous experiments conducted to test them, but none has come into general acceptance in its own right; a detailed review of this work was published recently (2). One of these hypotheses, the so-called "thermostatic" hypothesis, has provided the back-

ground for the study reported here. According to this hypothesis, satiety is brought about through the intermediation of the extra heat which is generated in the course of food assimilation and which is referred to as the specific dynamic action of food (3). This extra heat is presumed to produce an elevation in brain temperature of sufficient magnitude to stimulate certain postulated thermosensitive elements in the hypothalamus. Satiety then results through inhibition of feeding reflexes. An abrupt postprandial rise in skin temperature has been demonstrated in humans (4), but this in itself could hardly be judged as supporting the theory since it implies nothing in regard to brain temperature changes or in regard to cause and effect. That specific dynamic action is one of the intrinsic food factors responsible for satiety was the conclusion of Strominger and Brobeck (5) as a result of experiments with rats. They noted a tendency toward higher caloric intakes as the percentage of lard in the diet was increased up to 57 percent. Since the assimilation of dietary fats yields smaller amounts of extra heat than carbohydrates or proteins (6), the implication was that with diets high in fat content, satiety was delayed in proportion to their reduced specific dynamic action.

The experiments to be described were designed to determine the relationship between food consumption and changes in internal body temperature under conditions which would permit a reasonable test of the thermostatic theory. Twenty-one rats were used, each weighing 400 to 600 g. Both brain and rectal temperatures were recorded continuously for 2-hour periods in repeated measurements. These temperatures were recorded before, during, and after food consumption. Diets of varying composition were used. The animals were housed in a continuously lighted isolated room whose temperature range was 24.5° to 29°C during the entire

series, but which was constant to within 0.5°C during any one experiment. Intracranial temperature was measured by means of a calibrated bead thermistor (Fenwal CB 3252, 2000 ohms at 25°C) which was coated with vinyl and mounted with its leads on a plastic frame. Under Nembutal anesthesia the thermistor was implanted in the cranium through a burr hole slightly posterior to the coronal suture. The thermistor remained in position for the duration of the experiment. It was inserted to a depth of approximately 7 mm from the dorsum of the skull and fixed in position by means of fine screws through the plastic frame and the bone. No attempt was made to achieve an exact localization in any particular region of the brain. There were no signs of disturbances of the central nervous system in any of the animals after the implantation. The hypothalamus was deliberately left undisturbed in these experiments. For purposes of interpretation, it will be assumed that the recorded temperature changes were reflecting uniform changes throughout the entire cranium including the hypothalamus. After food intake had returned to preoperative levels, the animals were placed in wire-mesh cages designed to restrict movement and to facilitate temperature recording. In some of the animals at the time of placement in the cage, a similar calibrated thermistor probe was inserted into the rectum a distance of 2.5 cm and fixed in position with adhesive tape. The leads from the thermistors were connected through Wheatstone bridge circuits supplied with 1.35-v mercury battery power sources, and temperatures were recorded with a Grass (Model 5) polygraph. The thermistors proved to be sensitive to temperature changes of 0.01°C, and were stable throughout their use.

During the first 20 minutes and the last 40 minutes of the 2-hour recording period, the rats were without food. In the intervening hour, one of a series of prepared powdered diets was offered

Table 1. Mean daily intakes of the various diets expressed in terms of total bulk, dry weight, calories and expected specific dynamic action. Numbers in parentheses represent data obtained from matched animals which received all of the diets at different times.

Diets	No. of animals tested	Bulk intake (g/100 g body wt.)	Dry intake (g/100 g body wt.)	Calory intake (cal/100 g body wt.)	Calculated specific dynamic action of dry wt. intake (cal/100 g body wt.)
Basal	16 (4)	6.46 (6.57)	3.80 (3.87)	11.06 (11.25)	1.30 (1.32)
High protein	12 (4)	5.46 (5.48)	3.28 (3.29)	12.80 (12.86)	2.76 (2.78)
High fat	13 (4)	3.60 (3.36)	3.60 (3.36)	18.48 (17.34)	1.56 (1.46)
High carbohydrate	13 (4)	6.25 (6.19)	5.37 (5.30)	21.01 (20.28)	2.10 (2.07)