val, was also a control group for the reactivation group tested 15 days after the reminder (28 days after training).

Figure 2B is a composite of retention ratios of all groups tested after 2 days of training only ("original memory" function) or after 2 days of training plus a reactivation treatment ("priming") given either 13 (studies 1 and 3) or 27 (study 2) days after training ("reactivated memory" function). A one-way analysis of variance over all data points except that of the study-2 reactivation group indicated that ratios differed reliably as a function of retention interval ($P < .025$) and provided the error term for individual comparisons between means (Duncan's multiple range test). The latter indicated that the apparent increase above 1.00 in retention ratios in each function (Fig. 2B) was reliable; also, ratios of groups tested 8 (original memory function) and 19 (reactivated memory function) days after training did not differ from ratios of no-reactivation groups tested after retention intervals of 14 and 28 days, respectively. Regression analyses indicated that retention was a linear decreasing function of time since either training ($P < .005$) or priming ($P < .005$). Although the linear model provided a relatively poor fit in each instance, the intercepts and slopes of the two functions did not differ (t's < 1). Thus, forgetting of a reactivated memory followed the same temporal course as forgetting of the original experience.

Our findings confirm Campbell and Jaynes' (*2*) proposition that reinstatement is a potent mechanism through which experiences of early infancy can continue to influence behavior. An infant's reencounters with contextual aspects of prior training or an earlier experience can prime or recycle the remaining memory attributes and enhance access to them, alleviating forgetting which otherwise appeared complete weeks earlier. Moreover, a reencounter with the original context can maintain access to the target memory with the same efficacy as original training. Our findings also implicate reinstatement as the mechanism which, during infancy, facilitates the acquisition of the vast amount of learning characteristic of that period of development.

More generally, our findings support a distinction between availability and accessibility of information in memory and imply that failures to observe retention in infants should be discussed in terms of retrieval failures rather than memory deficits (*3, 4*). We think that procedures that improve accessibility to important retrieval cues will radically alter current views of infant memory (*11*) and that conditioning procedures, which permit a direct assessment of retention in infants, offer a promising means by which to bridge the gap between human and animal memory research.

CAROLYN K. ROVEE-COLLIER
MARGARET W. SULLIVAN
MARY ENRIGHT, DEBORA LUCAS
JEFFREY W. FAGEN

Department of Psychology,
Rutgers University,
New Brunswick, New Jersey 08903

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8. Because operant levels are typically doubled or tripled during acquisition, retention ratios of .30 to .40 usually indicate performance at operant level. A 3-minute period of nonreinforcement at the conclusion of initial training sessions does not typically extinguish responding in infants 11 to 13 weeks of age.
9. During the reactivation treatment, infants produced responses at a rate of 0 to 2 kicks per minute; operant levels are typically 8 to 11 kicks per minute. In the infant seat, infants rarely exhibit the vertical leg thrusts characteristic of conditioned responding; rather, their movements seem to be postural adjustments or horizontal squirming.
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Vertical Transmission of Acquired Ulcer Susceptibility in the Rat

Abstract. *Premature separation of rat pups from their dams greatly increases their susceptibility to restraint-induced gastric erosions. When prematurely separated female rats grow to adulthood and mate with stock males, their normally reared F_1 progeny also have increased susceptibility to restraint-induced erosions. Cross-fostering studies show that prenatal rather than postnatal factors transmit this susceptibility to the F_1 progeny.*

Experimental interventions during an animal's early development can result in modified behavior patterns, physiologic response characteristics, and susceptibility to disease that persist for long periods. For example, it was found (*1, 2*) that premature separation of rat pups from their dams increases their subsequent susceptibility to restraint-induced gastric erosion (RGE) (*3*). We now report that this increased susceptibility to RGE is transmitted to the F_1 progeny of female rats who are prematurely separated from their mothers in their own infancy. We also report that the increased RGE susceptibility of prematurely separated rats is transmitted to their progeny prenatally. To our knowledge, this is the first report of an altered susceptibility to a particular disease, acquired by an environmental manipulation during postnatal development in one generation, that is transmitted to offspring in the next.

Gastric erosions can be induced in rats by a combination of food deprivation and restraint. If rats are separated from their mothers at the customary time (postnatal day 21), approximately 10 to 20 percent develop gastric erosions during restraint on day 30. However, after premature separation on postnatal day 14, approximately 80 to 90 percent develop gastric erosions during restraint on day 30 (*2*).

To evaluate the RGE susceptibility of the offspring of female rats, we compared four groups of F_1 progeny (Fig. 1A). In the parent generation, ten litters were separated from their mothers on postnatal day 14 and ten on day 21. The females from each litter were then allowed to grow undisturbed to maturity. At about day 100, one female from each litter was randomly selected and bred to a stock Wistar male. Their offspring were separated from the mothers either prematurely (day 14) or at the usual time (day 21).

On postnatal day 27 all four groups of F_1 progeny were deprived of food for 26 hours and then restrained for 28 hours at an ambient temperature of 22°C. Afterwards the animals were killed and their stomachs examined for gastric erosions under a light microscope (×30). The experimenter was unaware of the origin of the stomachs.

The group of special interest was the normally separated progeny of mothers who had been prematurely separated in their own infancy. Sixty-four percent of

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these F_1 rats developed gastric erosions, whereas in the control group (normally separated progeny of normally separated mothers), only 19 percent developed erosions ($\chi^2 = 17.6$; $P < .001$) (Fig. 1B). If the F_1 rats were themselves prematurely separated, they had a high incidence (~ 80 percent) of gastric erosions, regardless of the early experience of their mothers (Fig. 1B). We conclude that a prematurely separated rat mother transmits her acquired RGE susceptibility vertically to her normally separated offspring.

In a second experiment we cross-fostered the F_1 progeny to determine whether the differences in RGE susceptibility among F_1 rats is acquired prenatally or postnatally. This experiment also served as a partial replication of the first experiment. The parent females were produced by the same procedure as in the first experiment. When about 100 days of age, two estrous females, each from a different litter, were mated at the same time with a single stock male. These mothers delivered litters within 24 hours of each other. After delivery the mothers from each pair of litters were switched so that all F_1 progeny were reared by foster mothers. On postnatal day 21 all progeny were separated from their foster mothers. On day 27 they were deprived of food and then restrained. (The animals were coded so that all rearing and testing was done without awareness of the experimental group to which each rat belonged.)

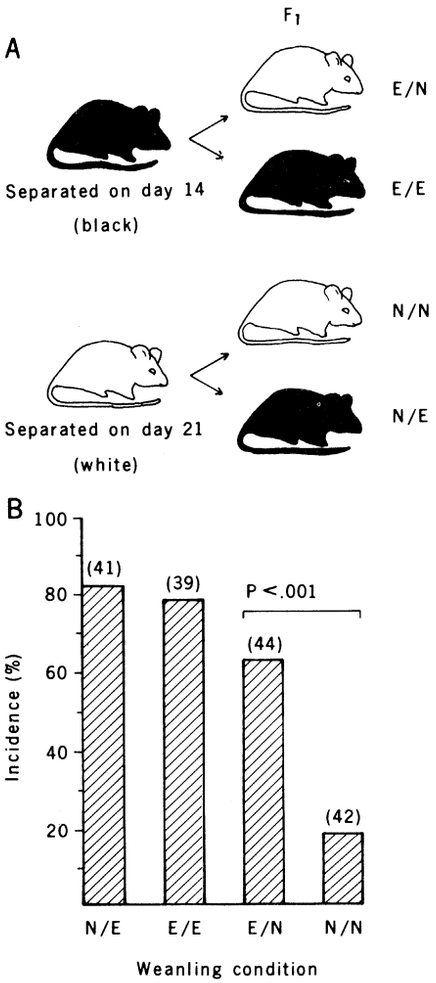

Fig. 1. Results of the first experiment. (A) Representation of the experimental groups showing their postnatal separation treatment. Abbreviations: *E*, separation on day 14; *N*, separation on day 21 (*E*/*N*, for example, denotes the normally separated F_1 progeny of prematurely separated mothers). (B) Incidence of RGE. Figures in parentheses give the number of F_1 rats tested in each group.

The incidence of RGE was 66 percent among F_1 rats born to prematurely separated mothers but reared by normally separated mothers ($E \times N$ in Fig. 2B). By contrast, the incidence of RGE in the rats born to normally separated mothers but raised by prematurely separated mothers was 24 percent ($N \times E$ in Fig. 2B) ($\chi^2 = 18.5$, $P < .001$). Thus the RGE susceptibility of normally separated F_1 rats is influenced by the early experience of their biological mother, not their foster mother. We infer that the increased RGE susceptibility associated with premature separation is transmitted to the F_1 progeny of female rats by prenatal factors.

In the course of conducting the cross-fostering study, we also evaluated maternal behavior by inspecting home cages twice daily to obtain scores for nursing, pup grooming, pup retrieving, huddling with pups, or avoidance of pups (*4*). Mothers who had been prematurely separated in their own infancy spent significantly more time away from their foster F_1 pups ($\chi^2 = 16.8$; $P < .001$) and less time nursing them ($\chi^2 = 13.0$; $P < .001$) than normally reared mothers. However, the results of the cross-fostering study (Fig. 2) show that these differences in maternal behavior do not contribute to the differences in RGE susceptibility observed among the F_1 progeny.

Among the experimental groups there are no immediately apparent differences that might explain the transmission of RGE susceptibility. Prematurely separated mothers are as fertile as normal mothers. Their litters are of the same size and weight at birth and survive equally well. Their progeny do not differ in weight up to day 28 and throughout the period of restraint. The individual weight differences observed in the F_1 rats could be accounted for by their own ages of separation and not by the separation experiences of their mothers.

There are analogous reports of an intervention before mating in female rats affecting both the animals and their progeny. Daily handling of unweaned rats is known to increase their activity and to decrease plasma corticosterone levels during open-field testing in their adulthood (*5*). Daily handling of unweaned females has also been reported to affect the open-field behavior (*6*) and plasma corticosterone levels (*7*) in their unhandled progeny. The exposure of female rats to various drugs before impregnation has been shown to affect their progeny. For example, the treatment of young female rats with trifluoperazine produces learning deficits in avoidance conditioning in both the treated rats and their untreated F_1 progeny (*8*). And the administration of thyroxine to neonatal female rats delays the time of vaginal opening and of first estrus in them and their untreated F_1 and F_2 progeny (*9*).

We know of only one other example of

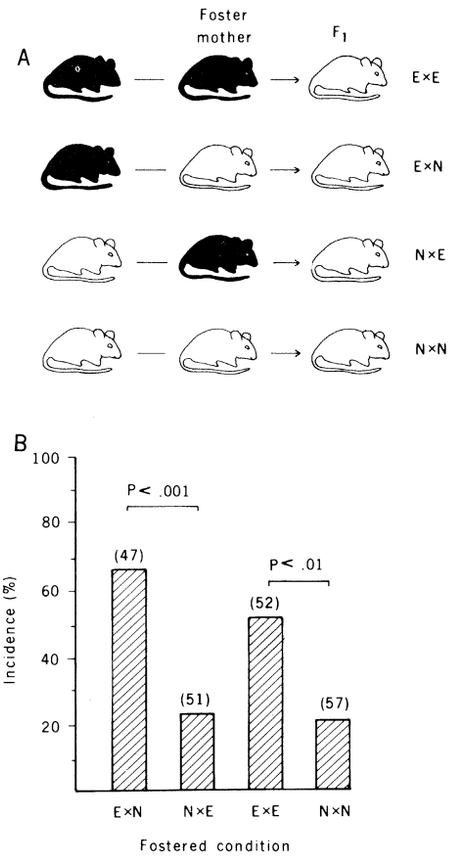

Fig. 2. Results of the second (cross-fostering) experiment. (A) Representation of the experimental groups showing their postnatal separation treatment. The left and middle columns indicate the separation treatment of the biological and foster mothers in their own postnatal periods. The right column indicates that all F_1 progeny were separated from their foster mothers on postnatal day 21. *E* and *N* (see Fig. 1) refer to the mothers of the F_1 test animals. ($E \times N$, for example, denotes that pups born to a prematurely separated mother were fostered at birth to a normally separated mother.) (B) Incidence of RGE.

a vertical transmission of an acquired disease susceptibility. A single subdiabetic dose of alloxan, administered to either a male or female rat before mating, has been associated with abnormal glucose tolerance in their untreated progeny (*10*). The degree of glucose intolerance was found to increase in successive (untreated) generations, leading to elevated fasting blood glucose levels in the seventh generation. However, our experimental results may be the first example of transmission of susceptibility to a disease in which the trait was acquired in the parent generation by an environmental manipulation rather than by a drug treatment. We know of no satisfactory explanation of this phenomenon.

NEIL J. SKOLNICK
SIGURD H. ACKERMAN
MYRON A. HOFER
HERBERT WEINER

Department of Psychiatry, Albert Einstein College of Medicine at Montefiore Hospital and Medical Center, New York 10467

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Saccades Are Spatially, Not Retinocentrically, Coded

Abstract. *Most models of the saccadic eye movement system imply that saccades are programmed for a certain distance and direction. Electrical stimulation of the brain was used to move the eyes of monkeys just before saccades to visual targets. Despite the stimulation-induced perturbation, saccades brought gaze to the target locations. This compensation indicates that saccades are coded to direct the eyes to a certain position in the orbit (or in space).*

When a target appears in the peripheral visual field, the eyes may make a rapid eye movement, or saccade, to bring its image onto the fovea. Most models (*1*) of the saccadic system assume that the oculomotor system attempts to minimize retinal error, the location of the image of the target on the retina relative to the fovea. The retinal coordinates of the target, computed by the visual system, could be used more or less directly by the oculomotor system to program a saccade with a particular amplitude and direction which will reduce retinal error. The saccade is thought to be ballistic, or programmed in advance for a certain direction and amplitude, since the movement cannot be modified or cancelled by visual information occurring later than about 50 msec before saccade onset (*2*). The superior colliculus, which has both retinocentrically organized visual and saccade-related neurons, has been suggested as a possible site for this sensorymotor interaction (*3*).

A number of deficiencies of the retinocentric models have been noted (*4*). Saccades can be made to the source of a sound in the dark or to a remembered target location in the dark (*5*). Clearly, a retinal error signal is not necessary to produce a saccade. Hallett and Lightstone (*6*) found that if a target is illuminated briefly during a saccade, the eyes will complete the saccade, and then look to the location of the target. Since eye movement occurred after target presentation, the correct localization of the target in space could not be due to a retinal error signal alone. They suggested that targets for saccades can be localized by combining eye position information with retinal error, although it does not follow that this is the usual means of defining the target location. Finally, the hypothesis that the amplitude and direction of the saccade is predetermined has also been challenged. Zee *et al.* (*7*) reported that patients with abnormally slow saccades can interrupt saccades in midflight in response to a new visual stimulus.

Robinson (*4*) and Zee *et al.* (*7*) have developed a spatial model of saccade generation based on these findings. In this model (i) targets for saccades are not localized relative to the fovea (that is, by retinal error) but rather by combining eye position with retinal error to form a representation of the target in space (*8*); (ii) the command to the saccadic generating system drives the eyes to a certain position in the orbit (*9*) and not just a certain direction and amplitude; and (iii) saccades are not programmed in advance but are directed to a final position by continuous feedback of eye position information.

We have attempted to test the retinocentric and spatial models by examining the interaction of visually elicited saccades and saccades produced by electrical stimulation of the monkey superior colliculus. Brief stimulation of the deeper layers of this structure produces an apparently normal saccade of short latency with an amplitude and direction largely independent of starting eye position or stimulation variables (*10*). The retinocentric and spatial models predict different outcomes if electrical stimulation drives the eyes away from the fixation point immediately before a saccade to a target. If, in preparation for a visually elicited saccade, the signal to the saccadic generator is a command to move the eyes in a certain direction for a certain distance, this movement should still be executed without modification just after the stimulation-induced saccade. In this case, the gaze will miss the target location by a distance and direction nearly equal to the stimulation-induced saccade. If the command to the saccadic system is a signal to move the eyes to a certain position in the orbit (or in space), the stimulation-induced saccade should produce an automatic readjustment of the vector of the visually elicited saccade so as to direct the gaze to the target location.

Two monkeys (a *Macaca mulatta* and a *Macaca nemestrina*) were trained to look at a visual target for a water reward. During training and stimulation sessions, the monkey's head was immobilized by a lightweight, permanently implanted head holder. The target was a small (0.1°) light spot on a short-persistence, large-screen oscilloscope (*11*) or a green light-emitting diode. Horizontal and vertical eye position was measured with a sensitivity of at least 0.25° through the use of an implanted electromagnetic search coil (*12*). A computer (PDP-8I) controlled the position of the target spot, triggered the electrical stimulator, monitored eye position, delivered reinforcement when tracking criteria were met, and produced on-line graphic displays of data and stimulus conditions. A description of the training procedures and apparatus has been published (*13*). The monkeys were

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