Infantile Experience and Resistance to Physiological Stress

It has been reported (*1*) that rats which had been "gentled" (that is, picked up and stroked once daily for 21 days postweaning) were heavier and reacted with less cardiovascular and gastrointestinal damage under conditions of immobilization for 48 hours than did the "nongentled" controls. In addition, adrenal glands of the nongentled were heavier than those of the gentled animals. Subsequent research (*2*) has revealed that rats handled prior to weaning showed significantly less mortality following 5 days of total food and water deprivation than did nonhandled rats or rats handled after weaning. The present experiment (*3*) was designed to investigate the response of rats, handled and nonhandled, in infancy (days 1 through 20) to physiological stress.

Twenty-seven male Sprague Dawley-Holtzman albino rats were handled from day 1 through day 20. Handling consisted of removing the pup from the nest, placing it in a 2.5- by 3.5- by 6-in. compartment, and then returning it to the nest. This procedure was followed once daily until weaning, on day 21. Twenty-nine rats were not handled in any manner through the first 20 days of life and then were handled only once, at weaning. The experimental treatments of handling and nonhandling were randomly assigned to complete litters. All rats within each litter received the same treatment.

All animals received no further handling until 70 days of age. At this time 20 rats from the handled group and 20 rats from the nonhandled group were given a 20-percent solution of glucose, injected intraperitoneally at a dosage of 7.5 ml/100 g of body weight, according to the method described by Brogi (*4*). A 21.4-percent mortality has been reported with this dosage for normal animals. Following the administration of the glucose, the animals were placed in individual cages without food or water. Twenty-four hours after the glucose injection the surviving animals were permitted to drink for 1 hour. The amount of water consumed was recorded. They were then sacrificed, and the left adrenal was removed and weighed. The remaining seven handled and nine nonhandled rats were not given the glucose injection but were sacrificed, and the adrenal weights were determined.

The mean body weight for the groups at weaning (21 days of age) was 47.74 g for the handled group and 44.34 g for the nonhandled group. This difference was significant beyond the 0.05 level. The mean weight for the groups at 70 days was 248.78 g for the handled group and 230.28 g for the nonhandled group. This difference was significant beyond the 0.01 level. These results are consistent with those previously reported (*5*) under identical conditions.

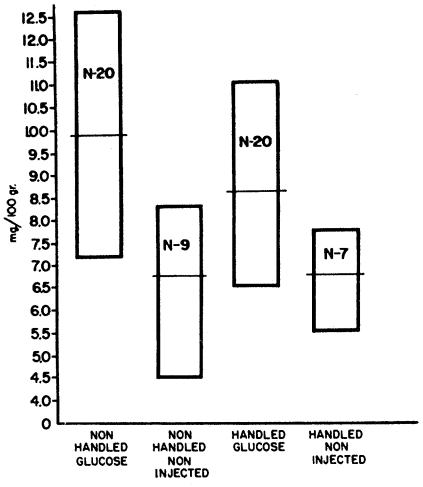

Fig. 1. Comparison of weights of adrenals of the various groups. The lengths of the bars indicate the range of individual values; the light lines, the means; and the numbers, the subjects within each group.

Although there was no significant difference in mortality between the groups following the glucose injection (three handled and two nonhandled rats died), there was a significant difference at the 0.02 level in the adrenal weights following the glucose injection. The adrenal weights for all the groups are presented in Fig. 1. It is important to note that, although the weights of the adrenals of the nonhandled animals were greater than the weights of those of the handled, both groups receiving the glucose injection had significantly greater adrenal weights than had their nonstressed controls. The noninjected groups had almost identical mean adrenal weights. Finally, the handled group consumed 4.29 g of water following glucose injection, whereas the nonhandled group consumed 2.11 g. This difference is significant beyond the 0.01 level. The difference between the handling procedure used in this experiment and the gentling procedure used by Wieninger should be recognized. Whereas Wieninger stroked and fondled his rats, the rats in this study were merely transported from the nest to a compartment and after 3 minutes were returned to the cage. That this procedure produces results similar, if not more profound, than those produced by the gentling procedure argues against the concept of "gentling" and the surplus meaning associated with this term as the major variable in the effects of early experience on behavior under stress in adulthood. It has been proposed (*6*) that handling constitutes a stressful situation for the infant organism and that early experience with stress results in a greater ability of the organism to adapt to psychological and physiological stress in adulthood.

Bovard (*7*) has suggested that, as a result of early handling, the threshold for emotional reactivity is raised. The present data suggest a more generalized hypothesis—namely, that the nonhandled animals are more profoundly affected by stress, both psychological and physiological. The greater adrenal weights of the nonhandled animals following glucose injection suggests a greater output of ACTH as a result of stress. The differences in the water intake may be a result of greater ADH production by the nonhandled rats following stress. Insofar as both ACTH (*8*) and ADH (*9*) have been shown to increase markedly following noxious stimulation, the hypothesis that handling in infancy reduces the physiological response to stress is supported.

Since ACTH (*10*) and ADH (*11*), and in general the stress reaction (*12*), appear to be mediated through the central nervous system, it is my belief that the effects of early experience modify later reactivity of the central nervous system under stress conditions. The precise nature of this modification is still unknown.

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References and Notes
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Inapparent Lymphocytic Choriomeningitis Infection in Folic Acid-Deficient Mice

Administration of amethopterin, or maintenance on folic acid-deficient diets, frequently causes mice to survive usually fatal lymphocytic choriomeningitis (LCM) infections, the virus being recoverable for long periods (*1, 2*). The experiments reported in this article deal with persistence of virus in treated mice having mild or inapparent infections.

Male mice from NIH stock were used, either Swiss "general purpose" or strain C57B1. The former, weighing 16 to 18 g when inoculated, were given bread-and-milk diets; the latter, weighing 7 to 9 g,