THE EFFECT OF RESERPINE ON THE CONDITIONED EMOTIONAL RESPONSE IN THE GUINEA PIG

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It is often revealing to contrast behavior of different species tested with similar procedures. Such comparisons may reflect the generality of a finding as well as emphasizing the unique adjustment patterns of the species. Accordingly, a comparison of the effect of reserpine on the conditioned-emotional-response (CER) phenomenon (Brady & Hunt, 1955) of rats and guinea pigs should provide additional information about the action of reserpine, the CER situation, as well as behavioral similarities and dissimilarities between the two species.

It has been repeatedly demonstrated that rats which have been trained to press a lever for food or water will stop responding during the presentation of a "critical stimulus" if the cessation of this stimulus has been associated with a painful shock (Estes & Skinner, 1941). Recently, it has been demonstrated that the degree of inhibition of lever pressing depends upon the temporal relationship between the duration of the critical-stimulus period and the interval between these stimulus presentations (Stein, Sidman, & Brady, 1958). The decrease in response rate during the clicker period has served as an objective measure of the degree of disruption of adaptive behavior resulting from "fear" or "anxiety" (Brady & Hunt, 1955).

Brady (1956) has shown that when rats are placed on a regimen of reserpine, they begin to respond at a higher rate during the periods of stimulus presentations.

The present report will describe results with the guinea pig when similar procedures are used. In addition, since guinea pigs have seldom been used in operant situations, an elaboration of special problems involved in using this species will be included in this report.

METHOD

Subjects

The subjects were 12 male guinea pigs, approximately 120 days old at the start of the experiment.

Apparatus

The experimental chamber was 15.5 inches long by 14.5 inches wide. The metal walls and the grid floor were wired for electric shock, and a retractable dipper presented 0.18 cubic centimeter of water for a 4-second interval. A large lever (2-inch metal tube, 1.5 inches in diameter with sealed ends) was used to prevent the animals from gnawing, a tendency which is very common among guinea pigs (Muenzinger, 1928). White noise was delivered continuously into the experimental room, and a clicking sound (critical stimulus) was presented through a separate loud-speaker.

Automatic programming of the experimental procedure and recording of responses was accomplished by appropriate relay circuitry.

Preliminary Training

Following 72 hours of water deprivation, the guinea pigs were trained to drink water from a large cup (0.5 cubic centimeter) which was made available at random intervals. The use of a large cup facilitated learning during the initial training. Guinea pigs over 500 grams are not endangered by 72 hours of water deprivation, and training is very difficult with shorter deprivation periods. A light placed just below the cup was lit as the cup started cycling and remained on as long as the cup was accessible. The experimental animals were left overnight in this training situation. Approximately 75% of the animals could be trained in this way to approach the cup rapidly as soon as it started coming up, and to drink from it while it was available. The remaining 25% was discarded, since some guinea pigs will sit motionless for such long periods that training is exceedingly difficult. On the following day, training to press the lever for water reinforcement was initiated. Because the guinea pigs does relatively little exploring in the testing chamber, it was found helpful to lure the animals to the lever with lettuce. Unlike the rat, the guinea pig does not synthesize Vitamin C, and fresh green vegetables which are rich in this vitamin serve as strong motivators. Lettuce was either tied to the lever or suspended above it. In the process of trying to obtain the lettuce, the animals pressed the lever; gradually, they learned to depress the lever to obtain water. The time necessary to establish the connection between lever pressing and the presentation of the water cup varied considerably. Some animals learned in the first session, while others took almost 2 weeks before they were responding regularly. The way the lever was pressed also varied. The strong tendency of the guinea pigs to bite the lever was circumvented by the use of a large-size lever, but most animals (9 out of the 12) learned to press with their chins. Unlike the rat, the guinea pig does not climb; therefore, a response which requires that the animal lift its forepaws off the ground is difficult to train. Depressing the lever with the chin proved to be a satisfactory instrumental response; but if biting is permitted, responses tend to occur in rapid bursts separated by pauses. Animals pressing with their chins were capable of much higher response rates than forepaw pressers.

Following three 2-hour sessions of continuous reinforcement, the animals were placed on a 60-second VI schedule.

Maintaining guinea pigs at an adequate deprivation level presented special problems. Food reward proved to be impractical because of the technical difficulties inherent in using a mash and the long consummatory time involved with pellets. Milk reward, which has proven satisfactory with rats, is not satisfactory with the guinea pig, since the adult guinea pig does not readily drink milk. In this laboratory, for example, a number of animals died from malnutrition while refusing to drink either condensed, evaporated, or whole fresh milk. In addition, it has been reported that diets of pasteurized milk cause guinea pigs to develop a calcification of muscles leading to a disorder known as "wrist stiffness," which interferes with locomotion and may result in paralysis (Wulzen & Bahrs, 1941). Still further, food deprivation as used in most laboratories requires that animals be maintained at a certain proportion of their body weight. The guinea pig, which may have a life span of over 7 years (Wilcox, 1951), in contrast to the rat, which seldom lives beyond 2 years (Farris, 1949), is growing at a very rapid rate at the age most likely to be used. With percentage of body weight as a guide, it has proven very difficult to keep the guinea pig both healthy and motivated for longer than several months.

Although water deprivation and reward was used, it also presents special problems for the guinea pig. In most laboratories, the Vitamin C requirements of the guinea pig are provided by a daily ration of fresh green vegetables (usually kale, lettuce, or cabbage). Because these vegetables contain approximately 80-90% water, the quantity provided must be controlled. Recently, the Ralson Purina Company has developed a special guinea pig chow which contains Vitamin C in a relatively stable state. With this special feed, healthy animals can be maintained with a minimum lettuce supplement (approximately 15 grams). This was given to the animals immediately after their daily testing. They received about 36 cubic centimeters of water (200 reinforcements from a 0.18-cubic centimeter cup) in a session. Because 600-gram guinea pigs will drink about 80 cubic centimeters of water when it is provided freely (Bruce, 1950), they were maintained at about one-half their normal liquid intake. When the animals were provided with approximately 250 grams of fresh lettuce following their Friday test, their performance on Monday did not differ from that during the rest of the week.

Conditioned-suppression Training

When the animals were performing at a steady rate for 5 consecutive days, a CER procedure was superimposed on the VI schedule. Every 12 minutes, a clicking sound was presented for 3 minutes; and simultaneously with the end of this stimulus, the animals were shocked through the grid floor. Shocking current was 2.0 milliamperes administered for 2 seconds. Testing sessions were 105 minutes and contained six stimulus-shock periods. After the animals were in the CER situation for 3 weeks, intraperitoneal injections of reserpine were administered at dose levels to be described in the following section.

RESULTS

Figure 1 illustrates the performance of a guinea pig on the VI schedule just prior to the initiation of the CER procedure, and 2 weeks later, when the animal's performance had again stabilized. This figure is typical of the performance of all 12 of the experimental animals except for two features: animals which pressed the lever with their chin responded faster than those pressing with their forepaws, and the length of time necessary to stabilize the performance on the CER procedure varied. The animals tended to stop pressing the lever for long periods of time following the first exposure to shock; and with three of the subjects, it was necessary to discontinue the CER procedure and to retrain them for several weeks on the VI schedule before reintroducing the stimulus-shock pairings. With these animals, responding on the CER procedure did not become stable for from 4 to 7 weeks.

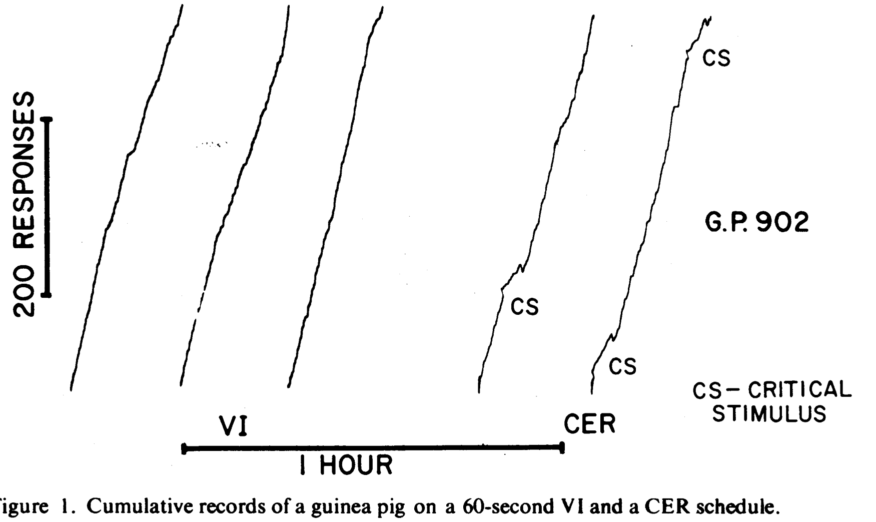

Figure 1. Cumulative records of a guinea pig on a 60-second VI and a CER schedule.

Several striking features of the guinea pigs' performance deserve special note. With the onset of the clicking sound (indicated in the figure by a raising of the recording pen), the guinea pig does not stop pressing the lever; rather, it continues to respond, although at a decreased rate. If the guinea pig is observed during this period, it can be seen that the animal presses the lever, but never drinks the water when it is available. Characteristically, the animal presses the lever, backs away from it, and remains motionless for several seconds at the rear of the testing chamber before advancing to press the lever again and repeat the cycle.

Figure 2 illustrates the result obtained following the administration of 0.003 milligram per kilogram of reserpine 22 hours prior to testing. The results of two typical animals are provided. The marked decline in response rate should be noted. The average decline in the rate for the 12 animals was 48% for this dose level of reserpine. Particularly striking is the almost complete cessation of responding during the clicker period (Fig. 2).

The effect of reserpine on response rates during the critical period can be seen by the following ratio: average response rate per minute in the clicker period over average response rate per minute during the nonclicker period. The average of the results of this ratio for the 12 animals yields a figure of 0.20 compared with 0.12 on the test following the administration of 0.003 milligram per kilogram of reserpine.

When other dose levels were administered, it became apparent that the guinea pig is extremely sensitive to small amounts of reserpine. Figure 3 contrasts the performance of a guinea pig 2 days prior and 3 days following the daily administration of 0.004 milligram per kilogram of reserpine. It can be seen that this small quantity of reserpine, when adminstered repeatedly, almost completely eliminates lever pressing. Another interesting re-

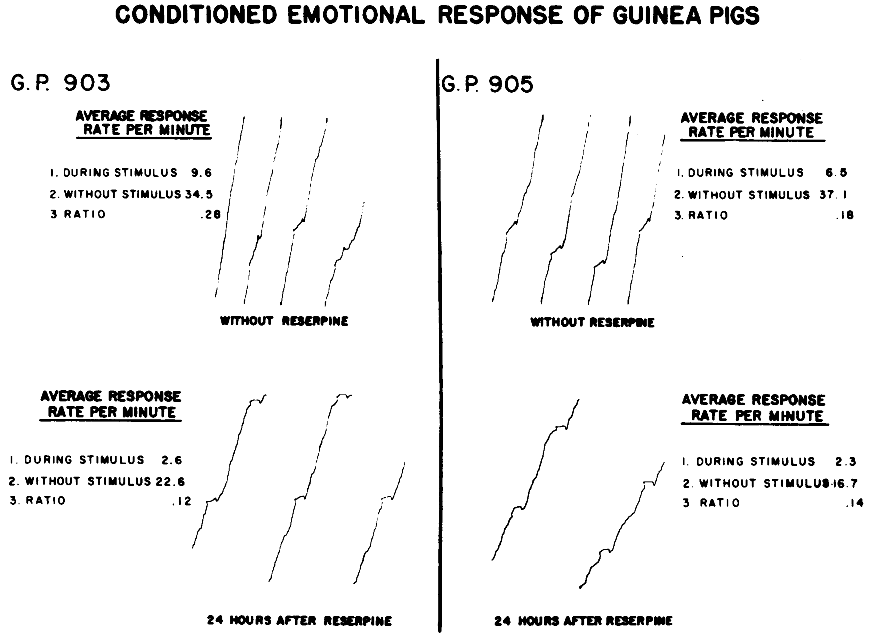

Figure 2. Cumulative records of the performance of two guinea pigs on a CER schedule before and after 0.003 milligram per kilogram of reserpine.

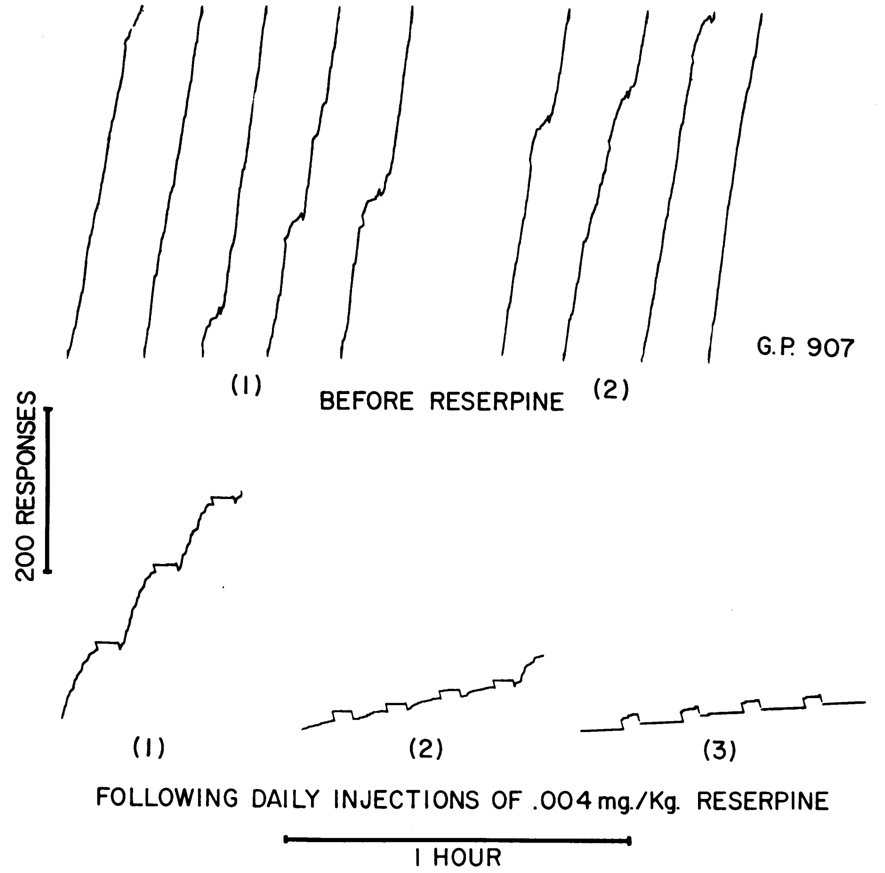

Figure 3. Cumulative records of a guinea pig 2 days prior to the administration of reserpine and 3 days following daily injections of 0.004 milligram per kilogram of reserpine.

sult is evident from an inspection of Figure 3. Frequently, when reserpine has almost completely suppressed lever pressing, the onset of the clicker serves to arouse the animal and results in short bursts of responding during this 3-minute period.

With single reserpine dose levels of 0.003 milligram per kilogram, the result was most generally of the first type described, i.e., a 50% decrease in lever-pressing rate during the nonclicker period and a marked diminution of responding during the clicker period. When the reserpine dose was above 0.03 milligram per kilogram for a single dose, or between 0.001 and 0.005 milligram per kilogram for 3 or more consecutive days, the animals almost completely stopped pressing the lever except for brief bursts during the clicker period.

DISCUSSION

Several interesting comparisons can be made between the behaviors of rats and guinea pigs in the CER situation. With the temporal parameters used, rats typically show a complete or almost complete suppression of responses during the presentation of the stimulus (Stein, Sidman, & Brady, 1958). The guinea pig, in contrast, continues to respond, although at a somewhat suppressed rate, but does not drink when the reward is available. There would appear to be a species difference in the response to "fear-provoking" stimuli. These results are in conflict with the statement that guinea pigs normally "freeze" upon hearing a sign of danger but run upon seeing one (King, 1956). While this specificity in responding may occur to predators in a natural setting, other studies have reported that under stress guinea pigs frequently show an intensification of the behavior in which they are engaged (Rey, 1936). Indeed, in the early stages of training, guinea pigs tended to freeze when frightened; however, after prolonged lever pressing, experienced animals normally continued to press when under stress. It is evident, however, that when contrasting species, a simple comparison of suppression of response rate during the critical period is not sufficient.

With the administration of reserpine, the rat typically presses at a higher rate during the critical-stimulus period (Brady, 1956), while the guinea pig, at least with the lower dose, presses at a significantly lower rate. It would appear that guinea pigs respond in a fashion similar to Blough's pigeons that were able to stand still longer under the influence of a tranquilizer (Blough, 1958, p. 587). One could appropriately substitute guinea pig for bird in his comment: "Since the birds were highly excited, one may appreciate at a common-sense level why a *tranquilizer* might enable the bird to *stand still* for an extended time." Here, again, is evidence that a simple quantitative analysis is not sufficient when comparing two species. While both the guinea pig and rat apparently were affected by the administered reserpine, their behavior in the CER situation changes in opposite directions.

With larger doses of reserpine or with chronic doses, the guinea pig's behavior is almost completely suppressed except during the clicker period, when short bursts are in evidence. It would seem that the clicker serves to arouse the animal to the point of responding. These results emphasize the fact that the stimulus may serve as both a warning signal and as an arouser. When an animal's general performance is suppressed as a result of a tranquilizer, the arousing aspect of the stimulus may, under certain conditions, play a larger role than its warning aspect.

Lastly, the sensitivity of the guinea pig to very small amounts of reserpine suggests that this animal may be of particular interest for further studies of reserpine action. With the guinea pig, single injections of 0.03 milligram per kilogram of reserpine would generally eliminate between 90-95% of all responding. In contrast, the rat was able to tolerate injections on the first day of 1 milligram per kilogram followed by 0.5 milligram per kilogram on the second day, and 0.1 milligram per kilogram for the remaining daily treatments with only a 50% reduction in rate (Brady, 1956). This finding is even more striking in view of the reports that the guinea pig has a very high threshold for chlorpromazine (Din, 1958).

SUMMARY AND CONCLUSIONS

Twelve guinea pigs were trained to press a lever to obtain water on a variable-interval schedule of reinforcement. A conditioned-emotional-response (CER) procedure, wherein the animals were shocked at the termination of a critical stimulus, was superimposed upon the VI schedule. Various dose levels of reserpine were administered. Results were contrasted with data from rats performing under similar conditions. The following conclusions appear justified.

1. With the temporal parameters used, rats tend to show complete, or almost complete, suppression of responses during the critical-stimulus period. Guinea pigs show only a partial suppression of response rate.

2. While rats typically remain immobile during the period prior to shock, guinea pigs can be observed to repeatedly press the lever and back away from it. While exhibiting this behavior the guinea pigs were never observed to drink water when it was available.

3. In comparison with the rat, the guinea pig was found to be extremely sensitive to very small quantities of reserpine. As with the rat, reserpine markedly decreased the lever-pressing rate of the guinea pig.

4. When reserpine is administered to rats and guinea pigs working in a CER situation, the effect is strikingly different. Rats, which normally are immobile during the critical period, start to press the lever in this period when under the influence of reserpine. Guinea pigs, however, normally press the lever during the critical period (although at a lower rate), but under the influence of reserpine tend to remain immobile.

5. The existence of species differences in behavior under similar conditions tends to highlight several features of reserpine action in the CER situation. These are discussed.

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