

Modification of the Conditioned Response Under Nembutal

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Allied Investigations.—Razran (12) indicates that the use of drugs in relation to the conditioning process is one of the important factors in experimental determinations of the nature of this phenomenon. Therefore it would be wise to examine some of the more significant studies which have been undertaken in recent years, especially those in which depressant drugs were used.

There has been some research into the effects of morphine in learning situations, but these have been mostly with rats in mazes (e.g., Macht (9)), or more generally with conditioning to the repeated injection of morphine (e.g., Krilov (7)). In most cases the level of learning was lowered and extinction was facilitated. The generalized physiological effects of morphine prohibits any precise conditioning work.

Curare is fairly well localized in its effect upon the organism and has been subjected to experimentation by Culler and others. Some very interesting results were obtained. It was found by Girden and Culler (3) working on dogs with buzz-shock conditioning, that a conditioned response established in a given muscle would disappear completely when the animal was under the influence of curare, to reappear when the normal state was again reached. Culler and others (2) repeated this experiment and found essentially the same results, concluding that “. . . under the influence of the drug learning occurs at subcortical levels, which are inhibited when the cortex returns to dominance.” (p. 272.)

Considerable Russian work has been done upon the effect of bromides upon the conditioning process. In general, the evidence is rather confused. Petrova and Usiyevich (11) say that individual variations to bromides (usually sodium bromide) are tremendous, but that in general a broad depression of behavior results, with larger doses being toxic and often fatal. But they say this, “Bromides are useful for developing differentiations, stabilizing extinctions, concentrating very generalized inhibitions, regulating delays in conditioned responses and preventing and curing experimental neurosis and hypnosis.” (11) (Razran's translation in Psychol. Abstr.)

The most common drug of the barbiturate class is the one used in this study, namely pentobarbital sodium. It is more commonly known by the trade name Nembutal. Tests by the manufacturers have disclosed that Nembutal is identical in its effect to its chemical isomer Sodium Amytal. For general use it is a fairly safe sleep inducer, with little or no other effects if used in moderate dosages. It is commonly used as an anesthetic and may, for the present at least, be purchased at any drug store. There is some evidence that it is a habit forming narcotic.

Williams (16), working with sodium-phenobarbital, a barbiturate derivative, found that rats so drugged displayed a marked tendency to

be inferior in maze learning, and in relearning, as measured by criteria of errors and time, than the control group.

Considerable work with Sodium Amytal has been carried out to determine its effect upon the behavior of psychotic individuals and a discussion of these properties is valuable in any interpretation that may be placed on more fundamental experimental work with animals.

Black and Groulund (1), Palmer and Paine (10), and Thorner (15) found in general that Sodium Amytal used in the treatment of schizophrenics was beneficial, though temporary, in most cases. It acted largely as an anti-inhibitory agent. Lindemann (8) found that with schizoids, a minute amount of Sodium Amytal, which in normal individuals gave no change at all, caused a lifting of the pressure which he feels tends to inhibit the stuporous patient from communication with others. He also noted that the delusional ideas and hallucinations present before the drug was given were not altered significantly.

Russell and Hunter (13), working with albino rats in a maze, using subcutaneous injection of Sodium Amytal in their experimental group, found that there was no clear indication that retention of a partially learned maze was any better or any worse in the drugged rats than in the normal group.

Settlage (14) did an investigation using twelve cats and both Sodium Amytal and Nembutal. His method was the bell-shock conditioning technique. Throughout his trials no animal exhibited any signs of development of conditioning while under the influence of the drug. He describes it thus:

"At the dosage listed the CRITICAL STATE phenomenon appeared, i.e., it was found that although there was no evidence of conditioning during the training period, learned modifications did nevertheless occur, since, when the effects of the drug has been partially or completely dissipated, conditioned responses could be elicited without further training. Thus the effect of the drug at the CRITICAL STATE was to inhibit the processes underlying the elicitation of the conditioning response without preventing the formation of new stimulus response connections." (14, p. 341.)

Statement of the Problem.—The present investigation was undertaken as an attempt to obtain more quantitative information about the learning process, as it is represented in the conditioned response method, and as it is affected by depressant drugs. Nembutal (Pentobarbital Sodium, Abbott) was selected and hypnotic dosages were used upon the dogs selected as subjects. The movements of all four feet and the respiration of the animals were recorded graphically to facilitate such quantification. Data so collected should fit into the large pattern of information concerning neural correlates of learning, and perhaps into the problem of movement and learning.

Experimental Method.—The experiment was conducted at the Indiana University Conditioning Laboratories. Six mongrel dogs were used. The conditioning technique consisted of placing a dog in a sound-proof room, in a specially prepared stock, with each foot fastened to a device which permitted the recording of movements of that foot upon a smoked record. Other connections with the dog were a pneumo-graph, electric

shock connection to right rear foot, and, within the room, a loud speaker, the onset or progress of each being recorded in the time sequence of their occurrence upon the smoked record. Behavior of the animal could be observed through a one-way screen. The training series trial consisted of the presentation of the conditioned stimulus for a period of two seconds, this being a 1,000-cycle tone, 50-55 decibels above the human threshold. During the last one-fifth second of this buzz-period a shock was also presented. The shock was direct current and was adjusted to the exact voltage necessary to elicit a flexion of the shocked foot equal to four inches, the limit the apparatus allows. This procedure, repeated at intervals of from 15 to 120 seconds, for twenty times, constituted a series. Five series, or 100 trials, were given during a single day's training session. A more complete description of the technique and training process will be found in a publication by Kellogg, Davis, and Scott (6).

Nembutal was administered interperitoneally in hypnotic dosage (one half the recommended anesthetic dosage). From one to two weeks were allowed after a day's training session to allow a complete recovery from the drugged condition.

Measures were made at the nine-fifths second point, or immediately before the presentation of the unconditioned stimulus, the shock. The number of observable and measurable responses at this point, obviously due to conditioning, in any given series of twenty, was expressed as the frequency. The height of the lift of the foot in question at this same nine-fifth-second point was measured and averaged for each series of twenty trials and is reported as amplitude. Other less important measures were also made, including latency and duration of response.

The plan of the experiment was simple. Each dog was given 400 trials, covered in four different, 100 trial, training sessions, each from one to two weeks apart. Three of the six dogs used were given hypnotic dosages of Nembutal immediately before the first and third of these training sessions. The other three were given Nembutal immediately before the second and the fourth sessions. In this manner it was sought to minimize so far as possible, by direct combination, individual differences in the dog (each serving as his own control) and the effect of order within the learning process.

Results and Discussions.—Notes taken of the general observed behavior of every dog for each training session indicate a similar pattern. The usual struggle patterns were exhibited for the first series or so of the control trials, but most dogs settled down before very many trials. The situation under drug was different from this, but a general similarity was shown. A very typical picture is shown in this memorandum of dog F27: "Given 4.1 cc. of Nembutal. Soon became very unsteady in walking, almost incapable of standing up. Other behavior, as snapping at other nearby dogs, response to experimenter, etc., seemed fairly normal, but dog exhibited a marked lack of muscular control, especially as it affected her balance. Unconditioned response was constant. After being taken from the stock, she could eat standing up but staggered a bit and frequently fell from her shelf."

A quantitative measure of the amplitude of lift, of the right rear, or shocked foot, was made from each trial. Amplitude was defined as the amount of measurable lift, to the nearest one-half millimeter, which occurs at the ninth fifth-second point; i.e., nine-fifths of a second after the beginning of the buzz, and immediately before the shock. The amount of such lifts in each series was *added together* and plotted as total amplitude for each dog. The number of such possible measures within each series was then used to obtain from this total amplitude the average amplitude for that series, and these results were plotted. However, the average amplitude curves were not significantly different to warrant inclusion, especially in the face of the slightly more indicative total amplitude curves.

If the total amplitude for all six dogs be combined for each of the ten series in which drug was given, in order, and a plotting of these values compared with a similarly derived curve for the values of the ten non-drug series, upon the same set of axes, we would have a picture of the progress of this measure throughout the learning process under drug, as contrasted to progress without drug. This has been done in figure 1, for the right rear feet only. The significance of these curves lies in the

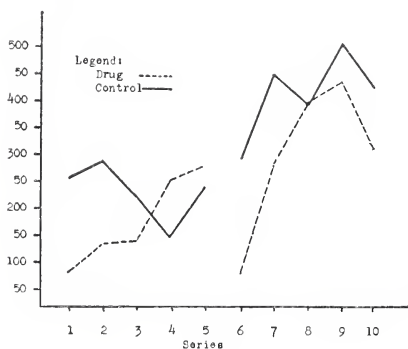


Fig. 1.

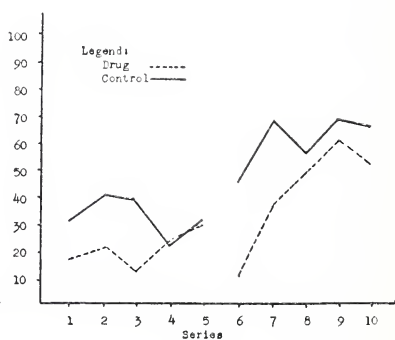


Fig. 2.

Fig. 1. Total amplitude per drug series, as contrasted with control series, for all dogs, in right rear foot only. Millimeters are represented on the ordinate.

Fig. 2. Curves showing absolute frequency under drug as contrasted with control training, for the right rear foot only. Percentages are expressed on the ordinate.

facts that: (1) there is an increase from beginning to end of the training, whether under drug or without; (2) the amount of this increase and the level which it ultimately reaches is, in general, less when the animals are under drug.

A second useful measure of the progress of learning in the conditioned response method is that of frequency. This was measured as the percentage, within a given series, of conditioned lifts occurring at the nine-fifth-second point. If now we proceed to combine the data so obtained, for all six of the dogs in terms of responses in each of the ten drug series, in order, and plot this on a graph, using the ordinate

as representative of the percentages of such responses, and the abscissa to represent the ten series, in order of their occurrence, within the drugged trials, it is then possible to plot on this same set of axes identically combined data for all six dogs for the ten non-drug trials. In so far as possible, this method of combining was aimed to minimize group differences and eliminate differences due to order of presentation of the drug, so that an ordered picture of the progress of the development of the conditioned response under the influence of the drug could be compared with progress without the drug, throughout the ten series in which no drug was given, and the same for the ten drug series. This has been done in figure 2. This combination indicates: (1) that the general curve of learning, in terms of frequency of conditioned responses, approximates a sigmoid curve, both with and without Nembutal: (2) that the level of learning is lower when the animal is under the influence of Nembutal.

Data were also collected on duration, latency, retention from one training session to the next, amount of shock necessary to elicit the unconditioned response, and on defecation and urination during training. Further information on these points and a more detailed discussion may be found in Headlee (5).

Summary and Conclusions.—Six unselected mongrel dogs, purchased from an animal dealer, were conditioned to lift the right rear limb by the buzz-shock method. Each dog was given training on four different days, separated by from one to two weeks, totaling 400 trials. In three cases, or one half of the group, a hypnotic dosage of Nembutal, administered interperitoneally, was given on the first and third days; in the other half of the group, three dogs, the drugs was given on the second and fourth session of 100 trials. Recording were made of the movements of all four limbs and the conditioned lifts of each of these limbs were measured and tabulated according to absolute frequency, total amplitude, and several other measures. Curves were drawn from these data to illustrate the progress of the animal during the training. These were combined in special ways to illustrate the contrasting behavior and progress with Nembutal and without it.

1. Qualitative observations indicate a general pattern of muscular unsteadiness, staggering, waxing and waning of established associations, consistent lowering of struggle behavior, yet ability to maintain unconditioned responses and to react to the immediate environment while under the influence of a hypnotic dosage of Nembutal.

2. The learning curve here found approximates the typical conditioning sigmoid curve.

3. The learning process could take place even under the inhibiting influence of a depressing drug, though at a lower level and rate with the drug, in this case Nembutal, a known cortical depressor.

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