Reports

Association of Conditionability with Degree of Reactivity in Psychiatric Patients

Abstract. A positive relationship exists between the number of times a subject responds with a psychogalvanic response to an orienting or alerting stimulus (tone) and the rate of learning in classical conditioning. This is seen by a correlation ($\rho = .65$ and .643 when corrected for ties) between the number of orienting responses and the resistance to extinction of the conditioned psychogalvanic response.

Pavlov believed that an association existed between temperament and conditionability. The belief is illustrated by his idea that the excitable or choleric type of dog readily developed positive conditioned responses (*1*). Pavlov's method of gauging excitability relied heavily on observations outside the experiment and apparently was not reliable. Spence and Taylor, however, have shown that "anxiety" as measured by a personality inventory is positively related to conditionability (*2*), and Franks has offered proof of the direct relationship between conditionability and a subject's position on an intraversion-extraversion scale (*3*).

As part of a study to determine whether groups of schizophrenics, depressives, and neurotics could be differentiated on the basis of conditionability, an attempt was made to see whether ability to condition could be predicted by objective measures other than diagnoses. The measure in which we were particularly interested was the unconditioned response to the conditioned stimulus—that is, the orienting (alerting) response. Such an orienting response usually drops out after the subject has been exposed to the orienting or conditioned stimulus a number of times, without temporal association with an unconditioned stimulus (*4*).

The subjects for this experiment were 67 in number; 25 manic depressives, 17 schizophrenics, 7 patients with chronic brain syndromes, and 18 psychoneurotics. At the time of the experiment, none of the subjects had received any specific treatment for his disease.

The stimuli used in the experiment were a tone of 500 cy/sec of conversational level (conditioned stimulus) and a mildly painful shock applied to the left ankle (unconditioned stimulus). The conditioned stimulus was generated by a Heathkit audio generator and was presented to the subject through a set of earphones; the unconditioned stimulus was generated by a Harvard coil connected to a 1.5-volt dry cell. The duration of the conditioned stimulus was 4 seconds, that of the unconditioned stimulus 1 second. In conditioning trials, the conditioned stimulus was followed immediately by the unconditioned stimulus. Psychogalvanic skin responses to these stimuli were measured with a Lafayette galvanometer and recorded, together with signals marking the stimuli, on a polygraph. An electronic timing device was used.

The subject sat in an air-conditioned, soundproof room and was observed, through a one-way-vision window, by the experimenters from an adjoining room. The procedure consisted of three phases. In the first phase (adaptation period), the conditioned stimulus was presented alone until the subject failed to give a measurable psychogalvanic response on three successive occasions or for a maximum of 30 trials; these trials are referred to as "orienting trials." The interval between each trial was varied in a random way between 30 and 60 seconds, and similar intervals were used in the other phases of the experiment. The second phase (conditioning period) comprised 11 paired presentations of the conditioned and unconditioned stimuli. The third phase (extinction period) comprised 15 presentations of the conditioned stimulus by itself. The three phases followed each other without pause, and the whole experiment lasted about 45 minutes. In the evaluation of the responses recorded, we used the latency of response from the time of onset of the stimulus to decide whether a given response fell into the categories "orienting response," "response anticipating shock," or "response to shock." We defined conditioned responses in the extinction phase as those responses which had the same latency with respect to the conditioned stimulus as the "response anticipating shock" and "response to shock" during conditioning. In this way the possible maximum number of conditioned responses during the 15 extinction trials was 30.

In order to determine the association of orienting responses in the adaptation period with conditioned responses in the extinction period, two measures of relationship were computed, a χ^2 test in which the data were dichotomized with the median number of responses constituting the cutting line for both the number of orienting responses and the number of conditioned responses during extinction, and a rank-order coefficient of correlation. The median number of orienting responses in the adaptation period was between four and five; the median number of conditioned responses in the extinction period was between three and four. Table 1 depicts the breakdown of the data subjected to the χ^2 test.

A χ^2 value of 10.96 was obtained from the data shown in Table 1, which is significant beyond the .01 level of confidence.

The rank order coefficient (ρ) of correlation between number of orienting responses and number of correlated responses in the extinction period was .65, and .643 when corrected for ties according to the method described in Siegel (*5*). This correlation is significant beyond the .001 level.

These results indicate a positive relationship between reactivity as measured by number of responses to a standard stimulus (tone) and number of con-

Table 1. Comparison of number of orienting responses in adaptation period with number of conditioned responses (CR) in extinction period. The median number of responses was used as the cutting line.

Four or more CR in extinction period (subjects)	Three or less CR in extinction period (subjects)
Five or more orienting responses in adaptation period	
24	9
Four or less orienting responses in adaptation period	
11	23

Instructions for preparing reports. Begin the report with an abstract of from 45 to 55 words. The abstract should *not* repeat phrases employed in the title. It should work with the title to give the reader a summary of the results presented in the report proper.

Type manuscripts double-spaced and submit one ribbon copy and one carbon copy.

Limit the report proper to the equivalent of 1200 words. This space includes that occupied by illustrative material as well as by the references and notes.

Limit illustrative material to *one* 2-column figure (that is, a figure whose width equals two columns of text) or to *one* 2-column table or to *two* 1-column illustrations, which may consist of two figures or two tables or one of each.

For further details see "Suggestions to Contributors" [*Science* **125**, 16 (1957)].

ditioned responses observed during the extinction period. Hilgard and Marquis (*6*) have noted that several studies point to negative correlation between conditioning and extinction—that is, that rapid conditioning is associated with slow extinction. In our study it was not possible to measure the conditioned responses in the conditioning period, for the giving of shock for reinforcement always gave a positive psychogalvanic response and the anticipatory response did not occur frequently enough by itself in the 11 conditioning trials to differentiate.

It is of importance to note that only certain orienting or conditioned stimuli offer the opportunity for this type of correlation. Reese, Doss, and Gantt abandoned the auditory conditioned stimulus because they found that the response to it took too many trials to decrease and disappear (*4*). In subsequent experiments they used a light as the conditioned stimulus, to which subjects made fewer orienting responses.

One other aspect of our data is of some importance: the relatively low medians for both types of response. The absence of a normal distribution of these responses suggests that there may be further ways of differentiating subjects.

GEORGE WINOKUR, SAMUEL GUZE, MARK STEWART, ERIC PFEIFFER, JOHN STERN, FRANZ HORNUNG

Department of Psychiatry and Neurology, Washington University School of Medicine, St. Louis, Missouri

References and Notes

1. I. P. Pavlov, *Lectures on Conditioned Reflexes*, W. H. Gantt, translator (International, New York, 1928).
2. K. W. Spence and J. Taylor, *J. Exptl. Psychol.* 42, 183 (1951).
3. C. M. Franks, *J. Abnormal Social Psychol.* 52, 143 (1956).
4. W. Reese, R. Doss, W. Gantt, *A.M.A. Arch. Neurol. Psychiat.* 70, 778 (1953).
5. S. Siegel, *Nonparametric Statistics* (McGraw-Hill, New York, 1956).
6. E. Hilgard and D. Marquis, *Conditioning and Learning* (Appleton-Century-Crofts, New York, 1940).

8 January 1959

Biochemical Responses of Rats to Auditory Stress

Abstract. Prolonged, intense auditory stimulation caused a marked reduction in glutathione levels in the blood of female rats. The frequency of the response was significant statistically and was related inversely to the recovery rate after auditory stimulation. An increase in adrenal weights and ascorbic acid, as well as a decrease in total adrenal cholesterol, were noted.

The present study explores alterations in certain biochemical parameters which were induced in rats subjected to repeated, prolonged, high-intensity auditory stimulation. Specifically, levels of blood glutathione, adrenal ascorbic acid, and total adrenal cholesterol are reported. The work extends the analysis of physiologic changes reported by other workers in the field of audiogenic stress (*1*). Hurder and Sanders (*2*) indicated that animals with larger adrenals were more susceptible to audiogenic seizures than animals with smaller adrenals. However, administration of adrenocorticotropic hormone (ACTH) did not affect seizure susceptibility. Blood glutathione index was employed as a possible indicator of "generalized" stress (*3*), since both cortisone and ACTH cause a transitory drop in the glutathione content in blood of rats and human beings (*4*). Present studies tend to indicate that the glutathione index may be a significant metabolic parameter in the investigation of psychoses (*5*). Both adrenal ascorbic acid and total adrenal cholesterol assays were employed as conventional stress indicators (*6, 7*).

Test and control groups consisted of Wistar female albino rats, weighing 145 to 195 g, paired by weight. The first test group was subjected to daily 1-minute intense auditory stimulation (frequency, 120 cy/sec; level, 100 ± 5 db) on 11 occasions, whereas, the second test group was exposed to daily 5-minute auditory stimulation 15 times. Although the animals were visibly disturbed when subjected to auditory stimulation, a seizure pattern was not induced. Control animals were subjected to the same handling procedures, excluding auditory stimulation. At the conclusion of the experiment all animals were killed with ether and autopsied, and the adrenals were removed immediately for ascorbic acid (*8*) and total cholesterol (*9*) determinations. Blood was obtained directly from the heart and assayed immediately for glutathione content (*10*). Hematocrit levels were determined to calculate the glutathione index.

Blood glutathione levels were reduced markedly in both test groups (Table 1) and *t* test analyses (*11*) indicated that the blood glutathione reduction in the 1-minute test group approached significance at the 5 percent level of confidence. Although the data for the 1- and 5-minute test groups are treated separately, to determine whether differences in duration of stimulation yielded different consequences, the combined test group data indicate a blood glutathione reduction (Table 1) which approached conventional levels of significance ($P = .07$). From the point of view of general consequences on biochemical indicators, the test data readily could be combined since the two test groups differed from each other only in the duration of the stimulus. Thus the experiment suggests that a drop in glutathione index appears as a result of auditory stimulation. To explore this possibility further, the glutathione data were evaluated on the basis of chi-square distribution (*11*). Even on the basis of the most critical frequency analysis, employing the combined test and control mean (glutathione index 73.5, 26 animals), 79 percent of the auditorily stimulated rats had values smaller than this mean, whereas 75 percent of the control animals had values greater. Despite the failure of *t* test procedures to yield a 5 percent significance level, chi-square distribution indicated a statistically significant effect ($P = .04$) with regard to the reduction in blood glutathione levels after recurrent auditory stimulation.

Table 1. Blood glutathione and adrenal ascorbic acid levels in female rats after prolonged auditory stimulation. The figures in parentheses indicate the number of values used in determining the mean. The Snedecor *t* test procedure (*11*) was used to determine the *P* values.

Blood glutathione index* (Mean ± S.E.)	Adrenal ascorbic acid content† (Mean ± S.E.)
Control	
80 ± 5 (12)	0.532 ± 0.020 (25)
Test‡	
64 ± 5 (6)	0.550 ± 0.038 (15)
$P = .07$	$P = .65$
Test§	
71 ± 5 (8)	0.579 ± 0.024 (12)
$P = .24$	$P = .18$
Combined test	
68 ± 4 (14)	0.563 ± 0.023 (27)
$P = .07$	$P = .37$

* Milligrams of glutathione per 100 ml of red blood cells.
† Milligrams of ascorbic acid per 100 mg of tissue.
‡ Stimulated daily for 1-minute interval, 11 days.
§ Stimulated daily for 5-minute interval, 15 days.

In addition, the blood glutathione data were evaluated and rated on the basis of the amount of locomotor activity exhibited immediately after discontinuance of the auditory stimulus. Preliminary findings suggest that the animals exhibiting the greatest locomotor response upon cessation of auditory stimulation had the lowest glutathione levels. This response relationship was not observed in the adrenal ascorbic acid or total adrenal cholesterol determinations.

Auditorily stressed animals of both groups had higher adrenal weights (*7*) and ascorbic acid values than controls (Table 1). Rats stimulated for 5 minutes had higher adrenal ascorbic acid values (8.8 percent rise) than rats stimulated for 1 minute (3.3 percent rise). This finding is in accord with reactions associated with chronically stressed animals or adaptation to a "continuously applied noxious stimulus," described by Sayers and Sayers (*6*). Adrenal ascorbic acid content would be greater in animals recovering or adapting to a repeated or a prolonged stress.