sponses of a given unit to sensory volleys scarcely vary in their latencies, but responses of some units occur about 20 msec following the responses of other units or recur about 20 msec after their initial responses. (iv) Application of strychnine causes repetitive discharge in nearly synchronous trains of approximately 85 percent of, but not all, the cells.

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Reliability of Activation Level during Adaptation to Stress

Abstract. This study points out the stability of a quotient expressing the recovery of basal skin resistance (BSR) level. Changes noted in BSR during stress are consistent with the behavior of tranquilized patients and have significance for drug therapy. Information of this type may be quite useful for interpretation and objectivity in a wide range of clinical researches.

To date, studies of the reliability of BSR measures have concentrated on work with normal subjects and tend simply to demonstrate adaptation after repeated exposure to the stimulus. The following study was primarily designed to appraise the reliability of the base-line adaptation of mental patients during stress. Basal skin resistance was the measure chosen since it is inversely related to sympathetic nervous activity or "activation level."

The subjects comprised two groups of 16 patients each, one group composed of 13 on various tranquilizers of the phenothiazine class plus three on Marsilid, an "energizer," and the other group consisting of nondrugged patients. Silver electrodes, stabilized by reversal of polarity every 3.1 sec, were applied to the palms of the patient's hands. The patient reclined on a couch and was instructed to look continuously at a Strobolux which was used to deliver a large field of flickering light from a distance of 7 ft. The Strobolux was turned on after a relaxation period of 10 min. Readings of BSR separated by ½-min intervals were made during the following periods: (i) 0.5 to 1.5 min, the initial resting period; (ii) 9 to 11.5 min; and (iii) 16 to 17 min. After a 3-day interval the procedure was repeated on each patient.

Two test-retest reliabilities were computed by using the following scores which were selected in advance of the data: (i) increase in BSR over the 7-min exposure to flicker, divided by the initial decrease in BSR due to flicker stimulation; (ii) increase in BSR, as above, divided by BSR just after Strobolux stimulation—that is, at 10.5 min.

Although the first of these scores is highly recommended in the literature for measuring the recovery quotient, its use gave insignificant reliabilities. The data strongly suggest that this is due to anticipatory activation during the second session. The use of the second score gave rank order correlations of .72 ($p < .01$) for both drugged and nondrugged groups and a total product moment coefficient of .78 ($p < .01$) for the combined groups. Considering that the second score compounds unreliabilities resulting from changes in adaptation and changes in BSR level at 10.5 min, the reliability is surprisingly high over a 3-day period when the anticipatory effects are taken into account.

A subsidiary experiment, an exploratory attempt at evaluating the validity of BSR measures of activation level, was conducted with data obtained from the above study. Casual clinical observations made by me and my associates on patients under the influence of tranquilizing drugs yielded general agreement to the effect that these patients were manifestly less aroused than those who were not receiving tranquilizing drugs. It was then reasoned that the manifest validity of BSR should be reflected by a higher resistance level for tranquilized than for nondrugged patients. Hence, the three patients on Marsilid were dropped from the drugged group along with three randomly chosen nondrugged patients. The subjects had been so chosen that it was possible to obtain balance or conservative bias with respect to the following characteristics; sex, race, diagnostic category, and manifest agitation (see Fig. 1).

The data were converted to log conductance units in order to approximate a normal distribution. An analysis of variance was made over drug categories for

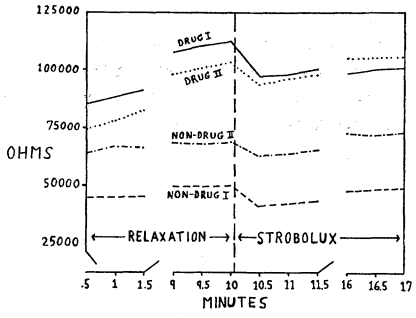

Fig. 1. Average BSR on drugged and nondrugged groups for sessions one and two

the initial resting period and over session number. Interaction and session number were not significant. Drug versus nondrug achieved an F of 9.63 ($p < .01$). A breakdown of this F by two t-tests, one for the first session which was significant at better than the 1-percent level and one for the second session which was not significant, suggested a further influence of anticipatory effects.

The three nondrugged patients were reincluded, and two exploratory hypotheses were tested *a posteriori*. It was found (i) that the change in initial resting level from session one to session two did not differ significantly for drugged or nondrugged groups, and (ii) that the change in BSR over the entire relaxation period was significantly different ($p < .05$) between drugged and nondrugged groups, the former showing a greater increase in BSR.

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Effect of Chlorpromazine on Salmonella enteritidis Infection in Mice

Abstract. Chlorpromazine increases the susceptibility of mice to infection with *Salmonella enteritidis.*

Goldman reports that infections are numerically among the most frequently encountered complicating factors in the institutional use of chlorpromazine and reserpine (*1*). He states that it is not believed that increased susceptibility to infections is a specific effect of these drugs. Experimental work with different species of animals and different pathogenic organisms has not led to consistent conclusions (*2, 3*). The following experiment was designed to study in a strain of mice the interaction between various dosages of chlorpromazine and the susceptibility to varying inocula of a virulent organism.

One hundred mice (Black Jax BAF 1 strain) of average weight 21.5 g were divided into ten groups of ten mice each. Chlorpromazine was administered subcutaneously in dosages ranging from 0 to 0.3 mg daily. Inocula of *S. enteritidis* in trypticase soy broth containing 0, 2000, 6000, and 14,000 organisms were administered intraperitoneally 24 hours after the first injection of chlorpromazine. The control groups, identically inoculated, were given daily subcutaneous injections of sterile water, and the noninfected, tranquilized control group received an intraperitoneal inoculation of sterile trypticase soy broth. Thus, as is shown in Table 1, the three groups of mice inoculated with 2000 organisms received 0, 0.2, and 0.3 mg of chlorpromazine, the four groups infected with 6000 organisms received 0, 0.1, 0.2, and 0.3 mg of chlorpromazine, and the two groups infected with 14,000 organisms received 0 and 0.1 mg of chlorpromazine a day, respectively. The noninfected control group received the highest dosage of chlorpromazine (0.3 mg) used in the experiment. The mice were allowed to eat and drink ad libitum, and no difference in the intake of food or water was noted between the various groups on chlorpromazine medication.

The effect of chlorpromazine on susceptibility to infection was evaluated in terms of the average number of days survived by mice in each group at the termination of the experiment—that is, 16 days after infection with *S. enteritidis*. After the 16th day no more injections were administered, although the mice continued to be observed for another 14 days, during which period no further deaths occurred in any of the groups. It was hypothesized that, should chlorpromazine be an adverse factor in the survival of the infected animals, the shortest average periods of survival would be manifest in the most heavily medicated group of the infected animals, and that the longest average periods of survival would be in the four control groups consisting of tranquilized, noninfected and nontranquilized, infected animals.

From the results summarized in Table 1, one can state that: (i) in the group given the highest dosage of chlorpromazine used, but no *S. enteritidis*, all survived the full 16-day period; (ii) for each level of *S. enteritidis* inoculation, increased daily chlorpromazine dosage shortened the average length of survival; (iii) at least for the two higher levels of daily chlorpromazine dosage, an increased quantity of *S. enteritidis* tended to shorten the average length of survival. The loading of survivors to the mean survival times can be estimated by consulting Table 2, which presents the frequency of survivorship for the same groups of mice.

Table 1. Effect of chlorpromazine on the average number of days (over a 16-day period) survived by mice following infection with *S. enteritidis*.

Chlorpromazine (mg/day)	Survival after infection (days)			
	No. of organisms			
	None	2000	6000	14,000
None		13.3	14.0	13.2
0.1			10.0	10.6
0.2		12.6	8.8	
0.3	16.0	10.0	8.5	

Table 2. Frequency of survivorship in numbers of mice which survived in each group of ten mice at the end of 30 days after infection with *S. enteritidis*.

Chlorpromazine (mg/day)	Frequency of survivorship			
	No. of organisms			
	None	2000	6000	14,000
None		6	8	5
0.1			3	3
0.2		4	2	
0.3	10	2	3	

An analysis of variance was performed on the days-of-survival data to test whether the differences observed might reasonably be attributed to chance. This resulted in an F value of 3.62, which, on 9 and 86 degrees of freedom, is significant at the .001 level (the estimated error variance was 16.7). The validity of the F-test is questionable, however, since the days-of-survival variable, by its very nature, tends to violate the assumption of similar group variances. (The group receiving no *S. enteritidis*, for example, has zero variance.) To avoid this objection, the days of survival recordings were ranked in order of magnitude, from 1 to 96, tied values being given the mean of the ranks tied for, and the Kruskal-Wallis H-test was performed on the resulting rank data (*4*). This yielded H of 27.09 which, treated as approximately chi-square with 9 degrees of freedom, is significant at the .005 level. Thus by either test there is little doubt that the differences observed in Table 1 reflect real differences attributable to the effects of the treatment combinations used. The survival data shown in Table 2 support this conclusion.

The mechanism for these observed actions of chlorpromazine is not clear. Blood cultures which were taken from the various groups of mice during the experiments showed an earlier onset as well as a more prolonged *S. enteritidis* bacteremia in the infected mice which were on chlorpromazine medication. A similar finding was reported by Maral and Cosar (*3*) in their work on tranquilized rabbits inoculated with pneumococci. Although this suggests some interference with the immune response of the organism, no individual factor can be singled out as the determining one. The reported effects of chlorpromazine medication include such findings as impairment in the function of the reticuloendothelial system (*5*) and depression of the phagocytic action of leukocytes (*6*). Whether analogous effects are obtained in the human being is unknown. However, at least one study has been reported in which the titer of antibodies to a hemolytic streptococcus was found to be significantly lower in patients on chlorpromazine medication than in a comparable nontranquilized group of patients (*7, 8*).

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