CPT[1] AND VCRT[2] PERFORMANCES AS FUNCTIONS OF IMIPRAMINE AND NIALAMIDE[3]

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PROBLEM

The present study was undertaken in comparative evaluation of Imipramine and Nialamide with a schizophrenic population showing depressive symptoms. Recent literature places emphasis on clinical and global behavioral evaluations of psychic energizers. A variety of psychological tests have been used for evaluating the effects of psychotropic agents. Behavioral rating scales and clinical evaluations are frequently used to evaluate changes in behavior and behavioral correlates of depressive syndromes. Basically, these studies have been aimed at assessment of reduction in symptomatology and therapeutic remission of depressed patients. Very often clinical judgment and observational techniques can be influenced by subjective orientations of clinicians and semantic inconsistency among observers. The present approach assumes that application of punctate measures in the areas of psychomotor activity such as attention and visual choice reaction time are more reliable techniques of assessing psychomotor changes produced by psychic energizers. Among depressive symptoms, psychomotor retardation is frequently very prominent as seen from a general clinical point of view.

There are numerous clinical reports on the improvement of depressed patients with Imipramine[2, 5, 6, 7, 10, 15, 18] and Nialamide[3, 4, 8, 12, 17, 19] in both psychotic and psychoneurotic depressions of hospitalized patients. Alexander[1] found that Nialamide produced a marked increase in conditioned psychogalvanic reflex response.

The major question of the present study deals with the effects of Imipramine and Nialamide on attention of schizophrenic patients as measured by the Continuous Performance Test (CPT) and the Visual Choice Reaction Time (VCRT) which was assumed to measure *S*'s preparatory set and ability to make simple discriminations. Primac, Mirsky, and Rosvold[11] tested normals *S*s on CPT after three and one half hours of Chlorpromazine administration. They found progressively poorer performance on the CPT as drug dosage increased. The CPT has been previously shown to be effective in measuring the effects of temperature as related to nerve chronaxy[9] and effects of brain damage on attention[14]. The advantage of CPT lies in that it requires continuous attention or alertness and is effective in isolating momentary lapses in attention. It also provides a measure of performance on tasks which vary in complexity, thus demanding different levels of attention. In this study, CPT and VCRT were used in assessing the effects of Imipramine and Nialamide therapy.

METHOD AND PROCEDURE

The patients selected for this study were 52 regressed schizophrenic patients with depressive features. These patients were selected by the psychiatric ward team on the basis of depressive symptoms characterized by at least three of the following features: (a) psychomotor retardation, (b) despondency-sadness, (c) lack of interest, (d) helplessness-pessimism, or (e) suicidal drive. All *S*s were under 50 years of age, and had not been treated with any antidepressive drugs for at least two months before the study, and were not suffering from any major physical handicap or organic brain damage. The *S*s were all billeted on the research ward where the milieu and the overall treatment programs were uniform throughout the study. The four treatment conditions

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[1]Continuous Performance Test.

[2]Visual Choice Reaction Time.

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were as follows: Imipramine (I), Nialamide (N), Imipramine placebo (IP), and Nialamide placebo (NP). There were 13 *Ss* assigned randomly to each of the four treatment groups. The drugs were administered for a period of six weeks, the dosages for each drug were as follows: first week, 50 mg.; second week, 100 mg.; third week, 150 mg.; fourth week, 200 mg.; fifth week, 300 mg.; and sixth week, 400 mg.. The medications were administered in two equal daily doses where dosage reached at least 200 mg. or more.

CPT. The CPT procedure was similar to the one described by Pishkin, *et al*[9], and was as follows: There were two series of letters, 36 each, mounted on a revolving copper drum. The drum was energized by an "Erector" electric motor powered by 110 volts AC. There were two tasks, X and AX, respectively. The drum revolved at approximately two revolutions per minute and was enclosed in a wooden case. The *S*'s task (X or AX) was determined by changing the horizontal position of the slot. On the experimenter's side of the apparatus were two automatic "Veeder-Root" counters which registered the right and wrong responses. The letters were illuminated by two .8 watt lamp bulbs mounted inside the case, one above each series of letters. The *S*'s task was to depress a telegraph-type response key placed directly in front of the apparatus. A correct response was recorded if the key was depressed within .76 sec. of exposure of the correct letter. Following the exposure of the letter, there was approximately .31 sec. before the next letter appeared. All *Ss* were given a practice period for the duration of one drum revolution. The X task was presented first. The *Ss* were instructed to depress the response key every time a letter X appeared in the slot. They were given this task for a 5 min. period. Following a 3 min. rest period, they were given a more complex AX task, also for a 5 min. period; this required response to letter X, only when it followed letter A. There were 10 and 6 correct responses per revolution possible for X and AX tasks, respectively. The total score was based on the number of correct responses produced in each task. The instructions varied somewhat from *S* to *S* in order to insure complete understanding of the task.

VCRT. The VCRT apparatus consisted of four 15 watt lamps with four corresponding keys mounted immediately under them. The *Ss* were instructed that when a particular light goes on, they were to depress the corresponding response key as quickly as possible. The four lights were not marked in any way. The lights and their corresponding keys could be symbolized from left to right as A, B, C, D. All *Ss* held their response finger in a white circle 2″ in diameter immediately below and between the B and the C keys. In a more simple reaction time procedure, the *S* was to respond to lights which were energized in the A, B, C, D order. On the first trial, *Ss* responded to signal light A, on the second to B, on the fifth again to A, etc. The A, B, C, D order was repeated 10 times. The duration of time between the onset of the light and depression of the corresponding key was reported as VCRT in units of .01 sec. The 3, 4, 5, and 6 sec. delays between the trials were randomly distributed over 40 trials to preclude anticipation of the signal light. The *Ss* responded with the right hand first for 20 trials and then with the left hand. The VCRTs were recorded by the experimenter after each trial.

The order of tests for all *Ss* was as follows: CPT (X), CPT (AX), VCRT (A, B, C, D), and VCRT (A, C, B, D).

Results and Discussion

Both the VCRT scores and the CPT scores were obtained before the patients were placed on their treatment regimen and after 6 weeks of treatment medication. The Wilcoxon[16] matched-pairs signed-ranks test was applied to test for the significance of differences between the first and the second evaluations on both tests. This test was especially useful for the present design, since it evaluates both the direction of the differences between first and second evaluation, as well as the magnitude of these differences. The analysis of the CPT test indicated that the performance of the N group significantly improved on both the X task ($T = 11$, $p < .01$), and on the more complex AX task ($T = 15$, $p < .025$). The mean numbers of errors on the CPT task for the four treatment groups are represented in Figure 1. No significant changes between first and second evaluations of performance on the CPT test were found with the other three groups (I, IP, and NP). The analysis of the Visual Choice Reaction Time shows that performance on this task significantly improved from the first to the second measurement ($T = 11$, $p < .01$) only with the N group. No significant differences were found in any of the other groups with a more complex (A, C, B, D) Visual Choice Reaction Time. The mean numbers of correct responses on the VCRT task are presented in Fig. 2, indicating a decrement in the Visual Choice Reaction Time on the A, B, C, D task for all the groups. It is noteworthy that performance improved on all groups, although not significantly, and this finding could probably be attributed to some savings in mastering the task from the first administration of the Visual Choice Reaction Time.

FIGURE 1. CHANGES IN CPT PERFORMANCE AS A FUNCTION OF FOUR TREATMENT CONDITIONS.

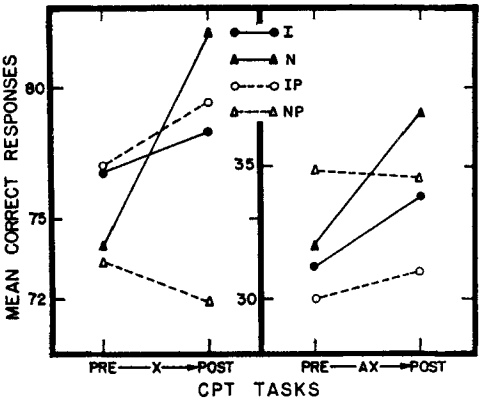
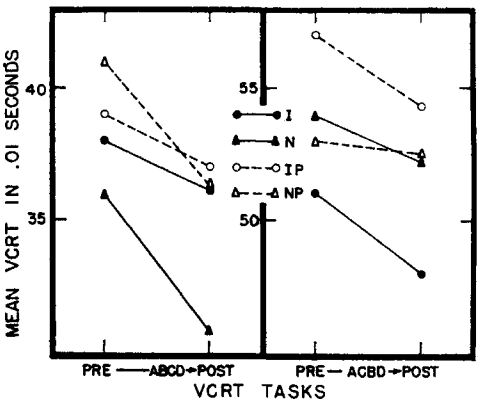


FIGURE 2. CHANGES IN VCRT AS A FUNCTION OF THE FOUR TREATMENT CONDITIONS.



The lack of significant improvement on A, C, B, D, may have been due to the relative difficulty of the task or fatigue, since this test was the last given to all the *Ss*.

Rothman, Grayson, and Ferguson[14] found that administration of Imipramine resulted in significant relief from depressive states. However, there were no motor correlates of this change in improving psychomotor functioning as measured by naming of words, color-naming, word-color naming, and figure 8 drawing. Present findings are consistent with the above, where there was no improvement on the psychomotor and attention factors as shown by CPT and VCRT with Imipramine. It is evident that psychomotor functioning is not affected by Imipramine, as it is significantly and positively influenced by Nialamide. From the present findings, it would follow, that although both agents have been previously shown to produce remission of depressive symptomatology, the concomitant improvement in attention and psychomotor "preparatory set" is not equal for both medications. The results of this study may have important implications for use of psychic energizers where patients may be expected to perform duties which may require sustained attention and alertness.

SUMMARY

Schizophrenic patients with depressive features were given Imipramine and Nialamide for a period of six weeks with gradually increasing doses. There were also two groups of patients who were given placebos to match the appearance of the two active drug agents. Continuous Performance and Visual Choice Reaction Time tests were given to all *Ss* before and after a six week treatment period.

The major findings were as follows: (a) The Nialamide group improved on both the simpler and the more complex Continuous Performance tests; (b) there was a significant improvement on the simpler Visual Choice Reaction Time in the Nialamide group; and (c) there were no significant changes attributed to the administration of Imipramine as measured by the two tests employed in this study.

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PHENOTHIAZINE EFFECTS IN CHRONIC SCHIZOPHRENIA*

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PROBLEM

Tranquilizers belonging to the phenothiazine family may induce clinical improvement in schizophrenic patients, yet differ somewhat in their action on specific target symptoms. Some of these drugs have been reported as differentially depressing the excitability of the ascending reticular formation and posterior hypothalamus. To the extent that behavior is dependent on the activity of these neuro-physiological systems, various phenothiazines may effect differing changes on components of psychological functioning. This study reports the effects of various phenothiazines on moderately chronic schizophrenic subjects' functioning in conceptual, perceptual and psychomotor functions.

PROCEDURE

Four widely used tranquilizers of the phenothiazine group, Chlorpromazine (Thorazine), Promazine (Sparine), Prochlorperazine (Compazine), and Perphenazine (Trilafon), were studied for their differential effects. Forty-eight subjects equally divided into these four drug groups and two control groups, each with eight subjects, were studied for twelve weeks. Drug and placebo patients were randomly selected from a larger group of moderately chronic patients who were to receive tranquilizers. Eight subjects who were receiving no phenothiazine medication during this period were similarly evaluated. All subjects had been prescribed tranquilizer following

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