THE EFFECT OF SMALL DOSES OF THONZYLAMINE, DEXEDRINE, AND PHENOBARBITAL ON TEST PERFORMANCE AND SELF-RATINGS OF SUBJECTIVE STATES* 1

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A. THE PROBLEM

In a previous article Landis and Zubin (2) presented the results of a study of the effect of fairly large doses of thonzylamine and phenobarbital. Their study was based on 72 subjects who ingested 150 mg of thonzylamine and 150 mg of phenobarbital in three doses during a 4½-hour period before starting the psychological tests. It was established that phenobarbital depressed the scores on a critical flicker fusion threshold test and on the speed and endurance scores on a simple tapping test while thonzylamine had no effect on the score of any one of the seven tests used. They also found that reports of the feeling state obtained by direct interview following each daily test period showed that both phenobarbital and thonzylamine produced a significant increase in the number of persons who felt “worse” or “different” but that the feeling was not related in any significant way to any change in score on any of the objective tests employed. Otherwise stated both phenobarbital and thonzylamine in fairly large doses tended to make the subject feel worse, but phenobarbital decreased the scores on three objective tests while thonzylamine did not affect the scores on any one of the seven tests employed.

The present investigation was concerned with the effect of smaller doses of thonzylamine, phenobarbital, dexedrine, and placebo on a self-rating scale and on five of the seven objective tests used by Landis and Zubin (2). The

*Received in the Editorial Office on December 13, 1951, and published immediately at Provincetown, Massachusetts. Copyright by The Journal Press.

*This experiment was undertaken at the suggestion of Dr. John Scudi. We are also indebted to him for much valuable advice. The Nepera Chemical Company provided the chemical agents studied and certain financial assistance which the writers gratefully acknowledge. Thonzylamine is a product of the Nepera Chemical Company which is marketed under the trade names of Neohetramine, Anahist, and Resistabs.

*Portions of the material here presented were submitted by R.B.C., in partial fulfillment of the requirements for the Ph.D. degree in the Faculty of Pure Science, Columbia University, 1950.
object of the present investigation was to determine whether small doses of phenobarbital and thonzylamine would affect the feeling-state, and whether the use of drugs of contrasting effects, dexedrine as a stimulant and phenobarbital as a depressant, would provide a clearer notion of the relative effect of thonzylamine.

The five tests employed were (a) choice speed test, (b) continuous problem experiment, (c) cancellation, (d) tapping speed test, and (e) critical flicker fusion. These tests were selected because they seemed to cover a wide range of psychological functions in a fairly systematic fashion. A self-rating scale was also used to indicate subjective changes in feeling-state on each day of the experiment.

B. PROCEDURE

Since thonzylamine is used in small doses at spaced intervals, a similar schedule of administration was followed in this experiment. The particular agents were administered four hours, two hours, and one-half hour before starting the testing. The testing was carried out in the early afternoon. Each person was tested at approximately the same time each day. The doses were either a quarter grain of phenobarbital, 5 mg of dexedrine, 25 mg of thonzylamine, or 5 grains of lactose (placebo). The dosage of the thonzylamine is that permitted by the Federal Food and Drug Administration for the "over-counter" sale of this agent as a self-administered cold remedy. The doses of dexedrine and phenobarbital are the usual doses prescribed by physicians when a mild stimulation or sedation is desired. These agents were all prepared by mixing each dose with lactose and making it into a 700 mg capsule. The capsules were of different colors so that each agent might be identified by the experimenters.

In order to circumvent suggestibility and the anxiety connected with "drugs," this experiment was designated as "A study of augmented vitamin effects." The subjects were told that we were investigating a possible effect on mental efficiency produced by vitamins when taken in combination with certain other chemical agents. In order to make our statement factual, we gave, together with each capsule of each agent a .25 mg pill of ascorbic acid (vitamin C). There is no evidence that 75 mg of ascorbic acid ingested during four hours has any psychological effect (4).

Twelve persons were tested during five successive days of one week and an additional 12 during five days of the following week. Twenty-one of the subjects were university students and the remaining three were university clerical employees. There were 18 males and 6 females with an average age of 25.5 years (range 18-37).
On zero day, between 8 and 10:30 A.M., the subjects were interviewed by a psychologist, examined by a physician, and given a pill box containing 3 placebo capsules and 3 vitamin pills. They were instructed when to take the capsules and pills and a time was set for each subject to report back for testing that same afternoon. During the afternoon, each subject was put through all the tests in order to acquaint him with the procedures. When he finished the tests that afternoon, he was given the necessary and appropriate capsules and pills in a pill box for ingestion on the following day, labeled as to the time that the doses should be taken. As a check, the subject was required to enter on the pill box the time he took each dose. On successive Days 1, 2, 3, and 4 he took the agents at the time directed and reported at a scheduled time for the tests which were administered in a regular order. The data collected on the zero day were not used in the calculations.

The following experimental design was used: Each subject took each of the four agents on one of the four testing days. Four things, A, B, C, and D may be arranged in 24 different sequences, hence, 24 subjects were used. Each subject went through a different sequence of agents and these sequences arranged themselves in such patterns that on each testing day there were four groups of six subjects—each group receiving a different agent.

C. Tests and Scales

The cancellation test, speed of tapping, choice speed test, and continuous problem task were administered and scored in the same fashion as reported by Landis and Zubin (2). The critical flicker fusion (Strobotac) test differed somewhat from the method used by Landis and Zubin in the following details. The intermittent light of a General Radio Company, Type 631-B Strobotac illuminated three circular test patches, each 3/4 inch in diameter, and one inch between centers. By means of appropriate colored glass interposed between the Strobotac and the test patches, the red-orange color of the neon lamp source was changed to an approximation of white light. Interposed between the Strobotac and the three patches were neutral density filters which differentially reduced illumination of the test patches. When measured just above fusion, the brightnesses of the patches were 0.45, 0.33, and 0.25 millilamberts. The patches were viewed binocularly at a distance of 10 inches. Each patch subtended a visual angle of about 1.5°.

At each experimental session and with each subject the Strobotac was first set a low rate so that all three patches seemed to flicker. The experimenter then slowly increased the frequency until the subject reported that the right
hand patch appeared steady. At this point the middle patch was seen by all subjects to be flickering somewhat while the left hand patch was flickering markedly. He was then directed to say when the center patch was more like the right than the left patch, then more like the left than the right, and so on. At all times, the left patch was flickering and the right patch was steady. In this way 10 determinations of CFF of the middle patch were made, five “ascending” and five “descending.” The score was the average of these 10 threshold determinations. This method has the advantage of presenting the subject with a flickering patch and a steady patch to which the test patch may be compared.

At the end of each day’s tests the subject rated his own feeling state comparing the way he felt at that time with the way he had felt the day before. Covering six steps labeled very, fairly, slightly, slightly, fairly, very, he rated himself for Happy-Depressed, Sleepy-Alert, Tense-Relaxed, and Interested-Bored.

D. Results

The preliminary analysis of the data for each test separately by means of the analysis of variance technique revealed certain trends, which were not strong enough to reach statistical significance. Believing that these trends might become more prominent if the elements common to all of the tests were extracted, a factor analysis (Spearman method) was undertaken to determine whether or not a central factor underlay the various tests. One factor was found which was sufficient to account for the common variance of all of the tests (Holzinger, 1). A similar factor analysis was made of the subjective ratings and here too one factor was found which would account for the common variance of all the ratings. The factor score for each individual on the day he had ingested each chemical agent was then computed for both the test performance factor and the subjective feeling-state factor. A comparison was then made between each pair of chemical agents for each individual on these factors scores. Table 1 shows the results of these comparisons.

The probability values in Table 1 were obtained by the exact method of computing probabilities of obtaining divergencies as large or larger than those observed under the null hypothesis of no difference attributable to the various agents (Pearson, 3). Any probability less than .05 is usually considered statistically significant. The fraction entries under N, for example 18.5, indicate a tied score. From the probability entries in Table 1 it is obvious that dexedrine factor scores, both performance and subjective, differ significantly in that they are higher, from those obtained after ingestion of thonzyla-
TABLE 1
THE NUMBER OF SUBJECTS EXCELLING ON THE PERFORMANCE TEST AND SUBJECTIVE FEELING-STATE FACTOR SCORE AFTER INGESTION OF EACH OF THE AGENTS WHEN COMPARED WITH EVERY OTHER AGENT, RESPECTIVELY

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Factor Score</th>
<th>N (1)</th>
<th>N (2)</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Dexe—2 Pheno</td>
<td>Performance</td>
<td>18.5</td>
<td>5.5</td>
<td>.0023</td>
</tr>
<tr>
<td></td>
<td>Subjective</td>
<td>12.0</td>
<td>6.0</td>
<td>.003</td>
</tr>
<tr>
<td>1 Dexe—2 Thonz</td>
<td>Performance</td>
<td>17.5</td>
<td>6.5</td>
<td>.01</td>
</tr>
<tr>
<td></td>
<td>Subjective</td>
<td>13.0</td>
<td>11.0</td>
<td>.27</td>
</tr>
<tr>
<td>1 Dexe—2 Plac</td>
<td>Performance</td>
<td>17.0</td>
<td>7.0</td>
<td>.01</td>
</tr>
<tr>
<td></td>
<td>Subjective</td>
<td>16.5</td>
<td>7.5</td>
<td>.02</td>
</tr>
<tr>
<td>1 Pheno—2 Thonz</td>
<td>Performance</td>
<td>12.5</td>
<td>11.5</td>
<td>.34</td>
</tr>
<tr>
<td></td>
<td>Subjective</td>
<td>15.0</td>
<td>9.0</td>
<td>.11</td>
</tr>
<tr>
<td>1 Pheno—2 Plac</td>
<td>Performance</td>
<td>14.5</td>
<td>9.5</td>
<td>.10</td>
</tr>
<tr>
<td></td>
<td>Subjective</td>
<td>11.5</td>
<td>12.5</td>
<td>.34</td>
</tr>
<tr>
<td>1 Thonz—2 Plac</td>
<td>Performance</td>
<td>14.5</td>
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</tr>
</tbody>
</table>

mine, phenobarbital, and placebo, with the exception of the Dexe-Thonz subjective, comparison. Phenobarbital, thonzylamine, and placebo are in no case differential in their effects on performance and subjective factor scores. Individual differences in susceptibility to the drugs employed probably accounts for the fact that the division was, for example, 18.5-5.5 rather than 24-0. It is also possible that, since the design of the experiment was such that six subjects took phenobarbital on Day 4 and dextedrine on Day 1 that these six would have higher scores on Day 4 due to the effects of the three previous days practice.

E. DISCUSSION

The simplest explanation of our failure to obtain significant differences on the mean scores on the individual performance tests of the groups of subjects who had ingested different chemical agents, namely phenobarbital, dextedrine, thonzylamine, and placebo is that any change on the part of any one person was obscured by the individual differences is susceptibility to these agents, particularly at the small dosages which we employed. Some persons may (or may not) have had their level of expected performance on these tests altered by these small doses. Probably any alteration which may have occurred in a majority of the subjects was obscured by the effect of day-to-day practice. In order to have found any significant differences in gain or loss beyond the daily practice effect it would have been necessary for a majority of the subjects to have shown a clear and unmistakable difference.
in score the day the particular agent was employed and for the daily variabil-
ity of the test to have been rather small. We employed dexedrine and
phenobarbital hoping to produce opposite or contrary effects. Although the
expected contrary effects of these drugs did not make themselves apparent in
the individual tests, they did influence the central core which underlies all
the tests—the factor scores. Thus, by cumulating the effects of the various
agents over all the tests, the influence of each factor was clearly detected and
the effect or lack of effect of each agent could be noted.

In brief we have demonstrated that the positive feeling state (happy-
relaxed-alert) reported after 3 doses of 5 mg of dexedrine had been ingested
exceeds that obtained when 3 doses of a quarter grain of phenobarbital was
ingested in 18 out of 24 normal persons. Thonzylamine at a dosage of 25
mg does not produce a depressed-tense-sleepy feeling state significantly more
frequently than did the placebo. Dexedrine led to an increased over-all
efficiency on the derived performance factor score when compared to each of
the other agents while neither phenobarbital nor thonzylamine effected this
score. Dexedrine gave an advantage on the performance test over the other
three agents but it did not differ by elevating the subject feeling-state score,
save when compared to phenobarbital.

Evidently the small doses employed (quarter grain phenobarbital and 5
mg of thonzylamine) were below the threshold of sensitivity of our five tests
and four rating scales. The effect of three capsules of 5 mg each of dexedrine
was above the threshold of sensitivity for both factor scores but below the
threshold for any single test or rating scale.

We may conclude that psychological tests do offer a means of testing the
effectiveness of a variety of chemical agents but that it is necessary to ad-
minister “above threshold” doses if clear results are to be obtained.

F. SUMMARY

The effect of the ingestion of small doses of thonzylamine, dexedrine,
and phenobarbital on five psychological test performances and on four self-
ratings of feeling states have been investigated. Twenty-four normal healthy
subjects ingested each of the agents. Dexedrine was administered in three
5 mg doses during four hours before the tests started. Similarly thonzyla-
mime was administered in three 5 mg doses and phenobarbital in three doses
of a quarter grain. A placebo of lactose was used as a reference point.
Special precautions were taken to circumvent the effects of motivation and
suggestion.

By a proper statistical manipulation of test results using the method of
factor analysis it was possible to derive a combined score from these five tests which gave significantly higher score following ingestion of 3 doses of 5 mg of dextedrine, showing that this dosage was just above the threshold of effectiveness for this group of tests. Thonzylamine and phenobarbital were below the threshold of effectiveness. Three 25 mg doses of thonzylamine during a four-hour period does not effect efficiency on these tests nor did it give rise to a depressed-tense-sleepy feeling-state while dextedrine did produce a happy-relaxed-alert state under the conditions of this experiment.

References


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