Published as a separate and in *The Journal of Psychology*, 1955, **40**, 53-60.

LYSERGIC ACID DIETHYLAMIDE (LSD-25): XI. CONTENT ANALYSIS OF CLINICAL REACTIONS*

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A. INTRODUCTION

Since the discovery of the psychic effects of LSD-25 (diethylamide of lysergic acid) by Hofmann in 1943, as reported by Stoll (4), there have been numerous experiments describing the effects of this drug. Symptoms such as trembling, anxiety, sweating of the palms, delusions, hallucinations, etc., have all been reported. However, systematization of the data leading to theoretical formulations still requires further investigation.

The purpose of this paper is to systematize and analyze the symptoms described by two different observers in 141 experimental sessions on 31 subjects with LSD-25.

B. METHOD

The subjects used were 31 non-psychotic adult volunteers who were paid for their participation. They were all of superior intelligence and exhibited considerable interest in the experiments. A more detailed description of the subjects is reported by Abramson *et al.* (2).

The raw data used in this paper were the summaries of symptoms reported to, or observed by the experimenters. These summaries were made by the two investigators separately on different subjects without collaboration. They did not anticipate that a content analysis would be made. They merely reported for the record their own observations. It is well to emphasize that there were two groups of subjects: those who took the drug and those who observed.

The experiments were conducted either in a pleasant office or in a protected

*Received in the Editorial Office on January 24, 1955, and published immediately Provincetown, Massachusetts.

[1]This investigation was aided by a grant from the Geschickter Fund for Medical Research. Dr. Kornetsky was assigned to the project by the National Institute of Mental Health, Bethesda, Maryland. He was stationed at the Biological Laboratory, Cold Spring Harbor, Long Island, New York. We are indebted to Sandoz Pharmaceuticals, Incorporated, for supplies of LSD-25 and other compounds.

laboratory environment. Subjects were administered LSD-25 orally in single doses up to 225 micrograms and observed for at least four hours. Nineteen of the subjects were used at more than one dose level. For convenience of analysis the data were grouped into six dose levels, zero micrograms (water), 1-25 micrograms, 26-50 micrograms, 51-75 micrograms, 76-100 micrograms and 101+ micrograms. The number of subjects at each of these dose levels was 20, 8, 25, 10, 15, and 6, respectively.

The analyses of the summaries were made by grouping the data into a number of arbitrarily selected descriptive parameters: *euphoria, dysphoria, distortions in perception, "neurotic,"* and *psychotic.* The signs and symptoms selected for each were:

1. *Euphoria.* (*a*) fatuousness, (*b*) laughter, (*c*) elation.
2. *Dysphoria.* (*a*) depression, (*b*) feelings of sadness.
3. *Distortions in Perception.* (*a*) auditory, (*b*) visual, (*c*) taste, (*d*) time.
4. *"Neurotic."* (*a*) nervousness, (*b*) anxiety, (*c*) inner trembling, (*d*) sweating, (*e*) moist palms, (*f*) palpitations-tachycardia, (*g*) difficulty in breathing, (*h*) trembling, (*i*) increased pulse rate, (*j*) feelings of hotness or coldness, (*k*) polyuria.
5. *Psychotic.* (*a*) hallucinations, (*b*) delusions, (*c*) depersonalization, (*d*) illusions, (*e*) dream-like feelings, (*f*) feelings of strangeness, (*g*) confusion, (*h*) suspiciousness, (*i*) uncommunicativeness.

The parameters selected are operationally defined by the symptoms reported; however, this does not imply a direct one-to-one relationship between such parameters as "neurotic" and psychotic with the diagnostic, nosological categories of neurotic and psychotic. Obviously the presence of some of the symptoms without others does not preclude a psychosis or a neurosis but merely states that these types of symptoms were more prevalent.

Following are the types of analyses made:

(*a*). The per cent of subjects manifesting one or more signs in any of the five parameters at each dose level was obtained by dividing the number of experiments, where one or more signs appeared at a given dose level, by the number of experiments at the given dose level for each subject. For example, if a subject was in two experiments at a given dose and in one of these, one or more signs appeared, one was divided by two giving a score of .50. These were then tallied and divided by the number of subjects at each dose level.

Rank difference correlation (3) was used throughout for the determina-

tion of the strength of relationship between the variables. The equation for ρ is,

$$\rho = 1 - \frac{6\Sigma d^2}{N(N^2 - 1)} \quad (1)$$

where Σd^2 is the sum of the squared differences between the ranks of the scores and N is the number of pairs of scores.

The standard error (σ_ρ) of ρ was determined by Equation 2:

$$\sigma_\rho = \frac{1.04\,(1 - \rho^2)}{\sqrt{N - 1}} \quad (2)$$

(*b*). For three of these parameters at each dose level the number of signs appearing was tallied for each subject. The mean number of signs for each subject was then obtained and these were totalled for each dose level and divided by the number of subjects at each dose level. Thus, the mean number of signs for each dose level was obtained for each parameter. Since the number of euphoric and dysphoric signs reported were so few, the mean number was not obtained.

C. Results

The relationship between each of the parameters and dose is illustrated in Figures 1 and 2. Figure 1 indicates that as the dose increases, there is a general increase in the number of subjects reporting psychotic-like phenomena and distortions in perception; however, there is not this positive relationship between dose and neurotic signs. The rank difference correlations (ρ) between dose and each of these three parameters are .94, .89, and .50 respectively, with respective standard errors (σ_ρ) of .06, .10, and .35. Figure 2 shows a non-linear relationship between the dose and euphoric signs with optimum euphoria appearing between 51 and 75 micrograms. Optimum dysphoria appears here between 51 and 75 micrograms.

If the mean number of neurotic signs and psychotic signs per subject are considered, the general picture changes only slightly (Table 1). Although

TABLE 1

The Mean Number of Signs for Each of Three Parameters at Each Dose Level

Parameter	Dose Level in Micrograms					
	Zero	1-25	26-50	51-75	76-100	101+
Psychotic	.05	.13	.60	.71	1.03	1.11
Distortions in perception	.45	.31	.98	.71	1.42	1.88
Neurotic	1.68	2.55	2.55	2.46	2.87	3.00
N =	20	8	25	10	15	6

there is more of a relationship between dose and neurotic signs shown in Table 1, the relationship is not as significant as between the other two parameters (psychotic and distortions in perception). It should be noted that the mean number of signs for each parameter is also a function of the number of signs selected for each parameter by the authors.

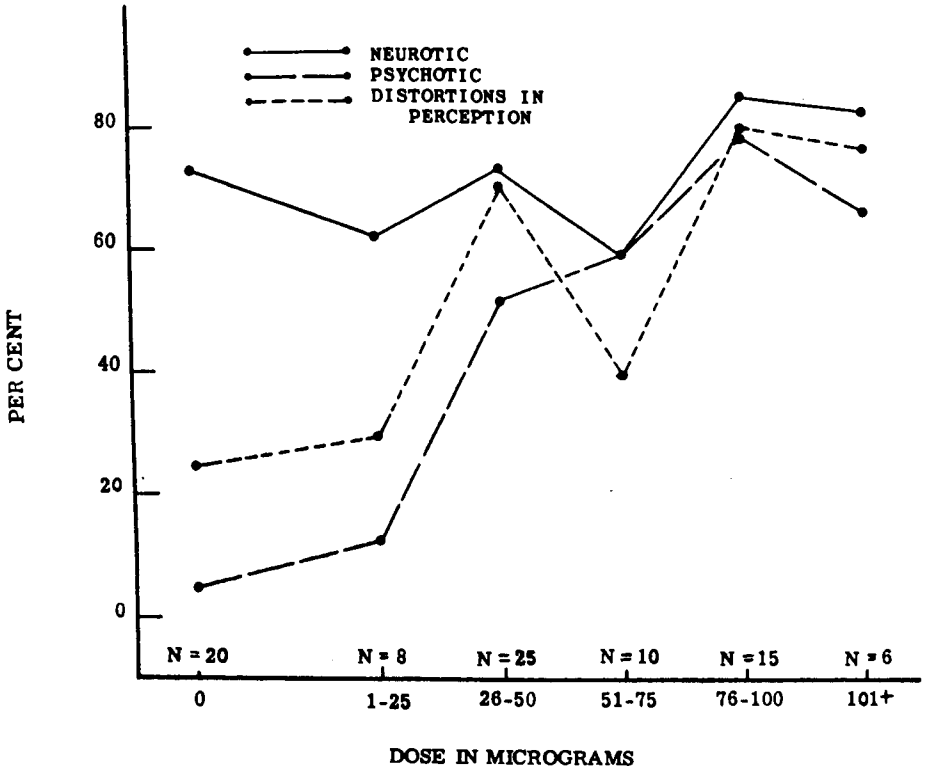

FIGURE 1

THE PERCENTAGE OF SUBJECTS MANIFESTING ONE OR MORE DISTORTIONS IN PERCEPTION, PSYCHOTIC, AND NEUROTIC SIGNS AT EACH DOSE LEVEL OF LSD-25

Computation of the relationship between the mean number of psychotic signs and mean number of neurotic signs for each subject under LSD-25 yields a ρ of .76 with a σ_ρ of .08. However, when correlations are computed between these two parameters at each dose level (Table 2), the relationship is only significant at the two middle dose levels.

Since neurotic signs are manifested quite frequently when a placebo is given (zero micrograms), it is of interest to determine whether or not there

TABLE 2

RANK DIFFERENCE CORRELATION BETWEEN THE MEAN NUMBER OF PSYCHOTIC AND NEUROTIC SIGNS AT EACH DOSE LEVEL

Dose level	N	ρ	σ_ρ
Zero	20	*	*
1-25	8	*	*
26-50	25	.61	.13
51-75	10	.92	.05
76-100	15	.31	.25
101+	6	.54	.33

*The number of subjects reporting psychotic signs was too small to analyze.

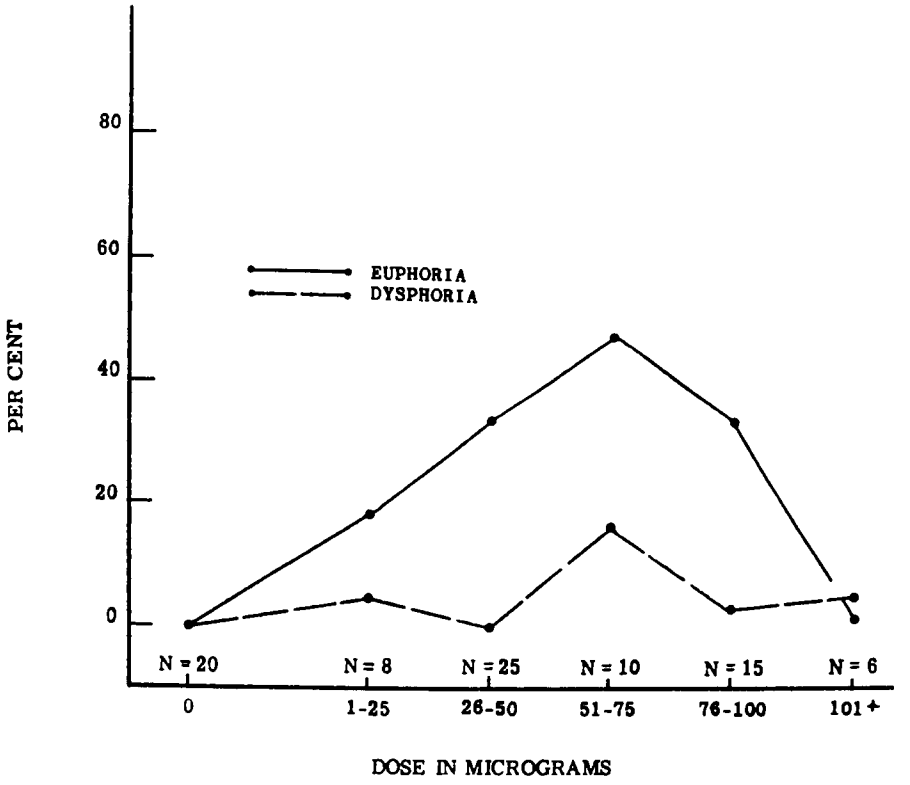

FIGURE 2

THE PERCENTAGE OF SUBJECTS MANIFESTING ONE OR MORE EUPHORIC AND DYSPHORIC SIGNS AT EACH DOSE LEVEL OF LSD-25

is a relationship between the number of neurotic signs at zero micrograms and the number of psychotic and neurotic signs subjects exhibit at higher dose levels. The rank correlation between the number of neurotic signs at zero micrograms and neurotic signs at greater than zero micrograms was .55 with a σ_ρ of .18. The value ρ between the number of neurotic signs at zero micrograms and psychotic signs at greater than zero micrograms was .21 with a σ_ρ of .25.

D. Discussion

Although the results indicate that three parameters, psychotic signs, neurotic signs, and distortions in perception correlate with the dose the relationship between neurotic signs and dose is relatively slight. Since the number of neurotic signs reported at zero micrograms is comparatively high and there is little correlation between neurotic signs and dose, it is suggested that the neurotic signs are not as much a function of the drug as they are of the situation and the personality of the subjects.

The data suggest that one could not predict with any great accuracy the relative frequency of neurotic signs that any individual may manifest due to LSD-25 from the number of neurotic signs at zero micrograms with the method of observation and reporting used. Moreover, it would be even more difficult to predict the number of psychotic signs from the neurotic signs at zero dosage. It appears that the anxious, suggestible person may not necessarily be the individual who will have the greatest number of psychotic symptoms. He is somewhat likely to continue to show neurotic symptoms, but he is no more susceptible to psychotic-like behavior than his less emotionally labile peer.

The finding of an optimum dose for the manifestation of euphoria is quite compatible with the reports of subjects who have been used at a variety of dose levels. In addition, this finding of an optimum dose for euphoria seems to coincide roughly with what is considered the optimum dose for the use of LSD-25 in psychotherapy (1).

Despite the apparent significance of the results they are presented as mere suggestive findings due to the following limiting factors.

1. *Validity of the Raw Data*

Whether or not any of these parameters measure what they are supposed to measure is arbitrary. These symptoms as reported are not objectively measured. The experiments were done in both a laboratory setting and a private office setting. Some of the summaries were culled from a questionnaire which asked about the absence or presence of these signs. In compiling

some of the other summaries, the investigators did not have the help of a questionnaire. There is the possibility that what is being analyzed is not the signs that the subjects manifest as much as the particular overt or covert hypotheses of the two investigators who compiled the summaries. Thus, the analysis presented may be merely the ferreting out of their particular hypotheses about the effects of LSD-25.

2. *Reliability of the Raw Data*

No attempt was made to determine the reliability of the data, since not enough experiments at the same dosage level were done on the same subjects to make a statistical analysis. Figure 3 shows the data for the mean number of neurotic and psychotic signs reported by each of the two investigators. Although Investigator *A* reports a greater number of psychotic signs

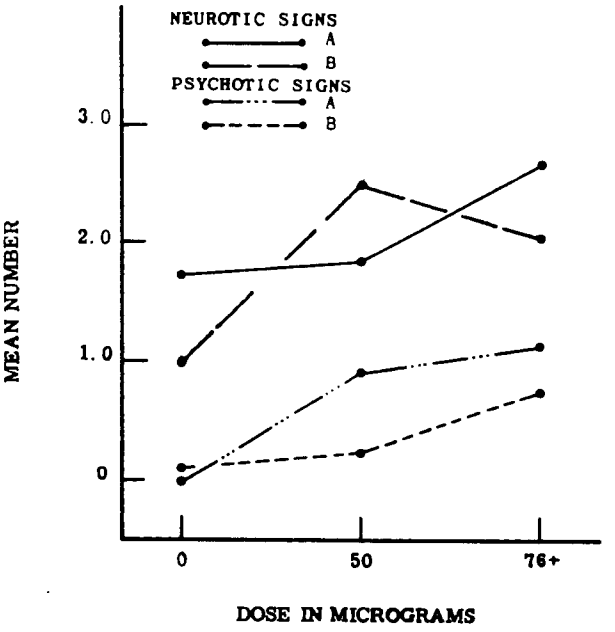

FIGURE 3

THE MEAN NUMBER OF NEUROTIC AND PSYCHOTIC SIGNS REPORTED BY EACH OF THE TWO INVESTIGATORS AT ZERO AND TWO DOSE LEVELS OF LSD-25

than Investigator *B*, the two curves are similar in shape. This, however, is not true for neurotic signs. *A* reported less neurotic signs at zero and 76+ micrograms than *B;* while *B* reported less signs at 50 micrograms. This

discrepancy, in part, may be the result of the specific effect of the drug on the individual subjects, rather than on any discrepancy in observations between the investigators since they did not report on the same subjects at the same time. The investigators wrote approximately the same proportion of summaries throughout the dose range. Therefore, the proclivities of each would be evenly distributed, and would not distort the shape of the curves.

E. Summary and Conclusions

A content analysis was made of the symptoms described in 141 experimental sessions on 31 subjects with LSD-25. The symptoms were categorized into a number of arbitrarily selected parameters. These were, *"neurotic," psychotic, distortions in perception, euphoria,* and *dysphoria.* The results suggested that:

1. Neurotic signs do not correlate with the magnitude of dose, while psychotic signs and distortions in perception do correlate with the magnitude of the dose.
2. There is an optimum dose for the manifestation of euphoria.
3. There is no relationship between the number of psychotic symptoms under the drug and the number of neurotic symptoms when a placebo is given.
4. There is only a slight relationship between the number of neurotic symptoms under the drug and the number of neurotic symptoms when a placebo is given.
5. At high doses of LSD-25, the subjects who manifest the greatest number of neurotic symptoms are not necessarily the ones who manifest the greatest number of psychotic symptoms.

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