THE EFFECT OF 1-ARYLCYCLOHEXYLAMINE (SERNYL) ON TWELVE NORMAL VOLUNTEERS

By

BRIAN M. DAVIES, M.D., M.R.C.P., D.P.M., D.C.H.

and

H. R. BEECH, Ph.D., B.A., Dip.Psych.

From The Bethlem Royal and Maudsley Hospitals

THE production of "model psychoses" in animals and man by a variety of chemical substances is of great interest. While the relationship between disturbances so produced and schizophrenia are problematical, these investigations may eventually throw light upon the causes of this condition. More important, at present, is the fact that the investigation of the way these drugs modify various aspects of normal psychological functioning is of great value in suggesting the physiological and biochemical processes that underlie these functions.

Sernyl is a new drug which has recently been investigated because of its psychotomimetic properties which limited its use in anaesthetic practice where it was originally used.

REVIEW

The search for an efficient intravenous anaesthetic led to a series of cyclohexylamine derivatives being synthesized and studied in the laboratory. These compounds produce a blocking of sensory impulses so that surgical procedures can be carried out without concomitant sleep and without significant depression of respiration and circulation. The first of the series to be investigated was 1-arylcyclohexylamine (Sernyl). Pharmacological studies on experimental animals showed that Sernyl has a local anaesthetic action approximately equal to procaine. It has no adrenergic blocking, ganglionic blocking, anti-cholinergic or anti-histaminic action and it produces no significant changes in respiration or blood pressure at non-lethal dosages. Its chemical structure, with the related compound cyclohexamine, and also pethidine, is shown in Figure 1.

It was shown, by observations on experimental animals, that Sernyl was a potent non-toxic drug. When 10 mg./kg. was injected into monkeys, a profound state of analgesia resulted and operations were performed without additional anaesthesia.

It was noted that "during the operations the animal had its eyes opened and looked about unconcernedly". Sernyl was then investigated as an anaesthetic agent in 64 patients by Greifenstein *et al.* (1958). It was found that at a dosage of more than 0·5 mg./kg. the patients became agitated, and at 1 mg./kg. rigidity occurred, followed by catatonia and convulsions. A dosage of 0·25 mg./kg. was found to be satisfactory and, in 30 of the patients, Sernyl was used as the only anaesthetic agent for operations that ranged from simple biopsies to gastrectomies. In the other patients, muscle relaxants and nitrous oxide were

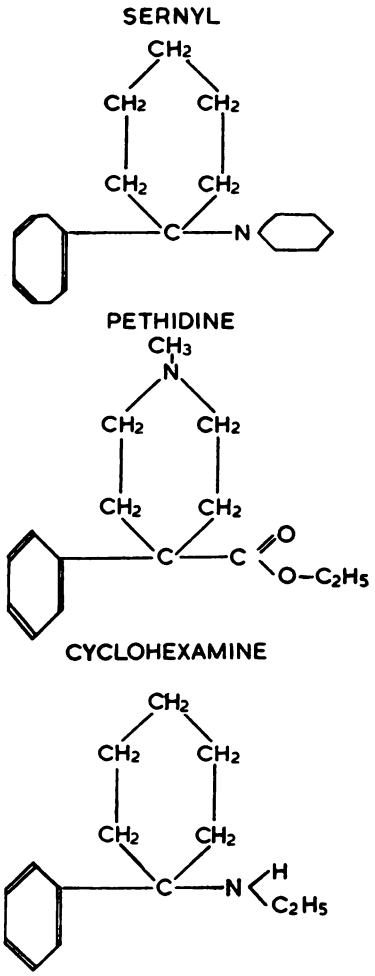

FIG. 1.—Chemical structure of Sernyl and related compounds.
(*a*) Sernyl.
1-(phenylcyclohexyl) piperidine monohydrochloride.
(*b*) Pethidine.
1 methyl 4 phenylpiperidine. 4 carboxylic acid ethylester.
(*c*) Cyclohexamine.
N-ethyl-l-phenylcyclohexylamine monohydrochloride.

also used. It was noted that, once recovered, the patients had no recollection of any painful stimuli during the operation; only the initial venepuncture was remembered then nothing more until they "came to". Unfortunately 10 of the 64 patients presented very difficult nursing problems in the post-operative period. They showed severely agitated, bizarre behaviour while echolalia and logorrhoea were also noted. Because of these reactions, the use of this compound in anaesthesia was discontinued by these workers, though another related substance, cyclohexamine, has been studied (Lear *et al.*, 1959) but again post-operative disturbances of a psychological nature are common.

Sernyl was then investigated by a psychiatric team from Detroit (Luby *et al.*, 1959). Sernyl was given intravenously at a dose of 0·1 mg./kg. to nine

https://doi.org/10.1192/bjp.106.444.912 Published online by Cambridge University Press

normal subjects and nine patients, four of whom were patients with chronic schizophrenic illnesses. In these schizophrenics, there was an intensification of the thought disorder and they became more difficult to manage. These behavioural changes continued for one month after the administration of the drug. The symptoms and signs produced by Sernyl in the normal subjects will be discussed later.

The sites of action of Sernyl are not known, though it is presumed to act selectively on the thalamus and mid-brain, producing impairment of pain, touch and proprioception. Meyer *et al.* (1959) reported further on the use of Sernyl as an anaesthetic agent and reported the electro-encephalographic changes seen after its administration. First there is a disappearance of alpha and beta activity, followed by a definite slowing, diffuse in nature but preponderant in the occipital, temporal and parietal regions.

Because of its action on the thalamus, Luby *et al.* (1959) have considered that Sernyl is an "interoceptive sensory blocking agent with psychotomimetic sequelae". They compared its action with results of exteroceptive sensory deprivation described by the McGill investigators (Bexton *et al.*, 1954) finding some similarities but "the disturbance in body image and the impairment in the symbolic process were far more severe with the drug than has been reported in any experiments during environmental sensory deprivation". These investigators also gave Sernyl to two patients under condition of sensory deprivation, finding that there was a greatly reduced verbal productivity, the experience being described as "sheer emptiness" as the volunteers were deprived of all external and internal stimuli.

With this background in mind, the aim of the present investigations was to study the effects of Sernyl from a psychiatric and psychological point of view on volunteers, then, from this pilot study, to suggest possible lines of investigation.

Material and Method

Sernyl was given to 12 normal volunteers—8 trainee psychiatrists and 4 psychologists. The drug was given in a quiet room, the subject lying comfortably on a couch. The first 8 volunteers were given 0·1 mg./kg. body weight by injection over five minutes. Vomiting, however, occurred in two volunteers and so the dosage was lowered to 0·075 mg./kg. At this dosage, the effects were still easily observed; vomiting, however, occurred in two more subjects. The subjects were told that they were to receive a drug that produced some psychological disturbances but no detailed information was given. It was realized that the suggestibility of our volunteers, all working in the field of mental disorders, and the expectant atmosphere of the experimental situation, could produce symptoms and signs. However, as the investigation proceeded, we became aware of a common central theme to each Sernyl experience, which we were particularly interested in. The occurrence of certain different accessory symptoms—e.g. anxiety, suspiciousness—were probably mainly dependent on personality factors and have not been commented on. (One subject was given two injections on separate occasions, one of sodium amytal, the other of Sernyl, in a random order. Observations suggested that one could be in no doubt as to which drug was Sernyl and that suggestion played little part in producing the gross effects observed.) Psychological testing was carried out before the drug was given, following which, the subject was asked to describe his experience for the first 10–15 minutes, when the testing was repeated, as it was on two or three subsequent occasions. Answers to proverbs were recorded on tape and analysed by

an independent judge, using standard criteria. Finally the subjects were asked to write down a description of their experience on the evening of the experiment.

OBSERVATIONS

To the observer, the Sernyl experience varied to some extent with each subject, yet the following account of the experience noted down as it occurred, contains all the essential features. (A more general account is contained in the next paper.)

Minutes	
0	Injection of 6·4 mg. commenced and given over five minutes.
2	"I feel as if I had had a few drinks—but not too giddy."
3	"I can't think clearly or easily."
4	"I feel a bit remote—I can hear—but I can't form my words properly. I feel a long way away—it's funny—but quite pleasant—it's odd—like a few whiskies—my voice seems to have a different sound to it—as if its reverberating."
5	"Your voice seems deeper—there is a hum in the room. I feel tired, as if I were falling asleep—your voice seems louder."
7	"It's strange—a sort of humming is heard—there is an odd feeling—I feel very tired—yet everything seems more acute—I'm sure I can hear a hum—like a reverberating hum—my voice sounds different."
9	"My limbs feel heavy and tired. That pin-prick is blunt—it just does not hurt—it's as if my senses are blunted."
11	"I don't feel able to control my movements properly—and the humming noise is still there."
12–20	Psychological testing carried out.
21	"My hand seems small—I can't seem to answer the proverbs properly—I feel as if I am talking from a long way away. I can't seem to think straight—I don't know why but I do know I can't do it."
22–30	Further testing.
31	"I feel a bit giddy—not unpleasant—it's difficult to describe—the pin is still blunt and my hands seem small—it's my fingers that are shortened and there is a vibration in all my fingers."
33–43	Further testing.
44	"My senses seem much more acute now. It's not pleasant, not unpleasant—I feel indifferent—and when I try and express things something stops me."
45	"I still feel that humming in my arms—like electricity."
46	"It seems so stupid—the proverbs seem stupid—I feel you are a long way away and I am indifferent to it—I can't think in a rational way."
48–60	Further testing.
61	"I feel more myself now but I am giddy when I move—it's better lying down."
62	Further testing.
75	"Things seem more normal now—the pin-prick feels sharper—things are now more acute."

Thereafter there was a gradual decrease in symptoms. At 100 minutes his hands appeared normal, and two hours after the injection, he was able to walk to the canteen for lunch, and he appeared normal to other people. He, himself, felt a little tired for another two to three hours and then was quite symptomless.

While the above could be taken as a typical example of the experience produced with Sernyl, in four patients "body image disturbances" were much more marked. Comments made at the time by these subjects were, "I feel very, very small—I'm tingling all over—small, small, small, going down—my hands do not look a part of me—it's horrible—everything looks narrow—it's odd—it's horrible—things seem a long way away—I feel numb all over—nothing feels part of me—it's terribly peculiar—you look miles away."

Another subject commented, "I feel to be floating away from everyone—it's unreal—things are distorted—you seem far away and bizarre—I seem to be floating off—I feel to be whizzing around, around and around—my hand looks distorted but it does not seem to be real—I feel detached from it all—I feel relaxed and my body detached and distorted from me. Everything has become enormous, fuzzy and one dimensional—flat—everything seems flat, as if cut out of cardboard—it's very bizarre."

One subject passed into a catatonic state. She complained of pins and needles in the limbs and face as the injection was given, and then for 23 minutes lay with her eyes opened, smiling, but unresponsive to questions. Then, at 23 minutes, she said, "Hullo—September—what is September?" Thereafter her account was similar to that described above.

While the acute symptoms subsided after 1–1½ hours, for several hours there was some unsteadiness on walking and most subjects felt generally "not quite right" for the rest of the day.

In four subjects, vomiting occurred—without nausea—and persisted for ½–3 hours.

Most subjects, for some hours after the experience, felt somehow detached from others and one commented, "Over lunch I had the odd feeling of lacking empathy with the whole human race—people's talk, their actions, lacked the genuineness and warmth of the old life." This detachment was commented on by several different observers who had dealings with the subjects later in the day.

Neurological changes occurred in each subject—there was a diminution of pain, touch and position sense. All showed nystagmus and were ataxic. One patient became diplopic.

The accounts produced for us during the evening of the experience show similar remarks, some of which will be added.

"I never really lost consciousness but sensations were viewed, somehow, from inside my skull—verbalization and evaluation were extremely difficult—then I felt like a flat worm—my head felt solid but below that I felt flat—like a huge skin rug—though if I looked at myself I saw in three dimensions. After a while, it all seemed a bit of a joke and I felt I had to entertain the tolerant audience."

"I can only account for very few thoughts—I do not know what happened in the first twenty minutes." (This is the subject who became catatonic.) "Thoughts seemed slow, quite clear, but isolated. Everything seemed unrelated and I lacked motivation to co-operate—I felt calm but without pleasure and I felt very slow about everything I did."

"The feeling was neither pleasant, nor unpleasant but peculiarly indifferent. Whilst I retained some insight—I could not think clearly on abstract

topics—my mental processes seemed slow and as well, there was an unwillingness to think, an indifference to the whole proceedings."

"There was a roaring sound in my ears—everything went round and round, then things looked very strange—flat—one dimensional—I felt remote, with a feeling of loss of emotional contact. My body felt huge and lifeless—my hand seemed remote, huge. At one moment there was a terrifying feeling of impending dissolution—I could not think actively, organize, relate in any way—I could not discriminate what to attend to. I also felt rather truculent and somewhat disinhibited."

"I had a feeling of falling down and getting smaller and smaller at the same time. When asked to open my eyes the room did not seem noticeably to have changed its size, but during the experiment, the nearest experimenter appeared to be a rather odd shape and size, his face especially seeming out of proportion and not similar to how I had previously seen him. I had to keep touching myself —my face, arms and hands. I knew they were mine and still there, but they felt very odd and as though they did not belong to me. I became very frightened of my hands at one point—they seemed very thin, bony (old) and apart from me. Another time my arm really felt very 'narrow' and made up of only two bones."

"There was no adequate ability to analyse a problem, break it down into component parts and then consider these serially—a series of words presented for learning were accepted as a temporal series but the ability to learn them in the sense of forming meaningful connections between words was totally lost."

"It is very difficult to account for the whole hour of the experience. I remember the injection, then I felt confused and 'delirious'. I remember repeating things and having difficulty in following what I was asked to do. I seemed to come back to normal in waves. Later that day I felt listless, affectless and, later still, my head felt muzzy and this was made worse by movement."

To sum up, the cardinal features described by Luby *et al.* (1958) were all observed—i.e., body image changes, estrangement, disorganization of thought, negativism and hostility, drowsiness and apathy, hypnagogic state, feeling of inebriation. Finally it may be noted that, except for the subjects who vomited, the experience was not unpleasant and most subjects were willing to repeat it if required.

Psychological Testing

The selection of psychological tests was determined by three considerations. First as objective checks on clinical observations of reactions to the drug; secondly by diagnostic considerations; and thirdly as a means of comparing reactions to Sernyl and barbiturates.

These tests were usually administered before the drug was given, some fifteen minutes after the injection, and at subsequent intervals up to 1½ hours after the injection. No individual was given the complete battery of tests.

Size Estimation

Two tests were employed in obtaining size judgments. The first of these comprised 7 cards (5 inches × 3 inches) each bearing a single circle. Only one of these circles was the diameter of one penny; three cards bore circles which were 2, 4 and 6 mm. larger, and three bore circles which were 2, 4 and 6 mm. smaller than one penny. The subject's task was to identify the card bearing a circle of the same size as one penny.

A similar task, involving identification of a card bearing a line one inch long, was also employed.

The data reported in Table I was obtained both before and 20 minutes after the injection.

TABLE I

Size Estimation

Condition	Plus	Zero	Minus
Non-drug	7	4	1
Drug	9	3	0

"Plus" indicates a judgment erring in the direction of choosing a stimulus larger than one inch or one penny. "Minus" indicates the opposite tendency. "Zero" indicates a correct judgment.

This data, obtained on six individuals, suggests that both in drug and non-drug conditions, there is a tendency to make errors of over-estimation of size. Omitting the "minus" entries and computing χ^2 for "plus" and "zero" entries under the two conditions, indicates that the trend further to exaggerate the tendency toward over-estimation under Sernyl is non-significant.

Area of Motor Response

A further effect, which may be related to size-over-estimation, is that of area covered in handwriting. This effect was examined in four individuals both before and after drug administration, when they were asked to write their full names and the words "United States of America". A rough index of area covered was found to be the overall length of the words written.

Three out of the four S's showed marked tendencies to increase the area of writing; the remaining subject showed slight changes in the opposite direction.

Tapping Speed

There is considerable evidence that slowness, both cognitive and motor, is produced by mental disorder (Foulds, 1951; Huston and Shakow, 1937; Nelson, 1953; Shakow and Huston, 1936). One might, therefore, reasonably expect that administration of Sernyl, if it produces some of the dysfunctions characteristic of schizophrenia, would result in impairment in motor speed and, in particular, that tapping speed will show decrement.

The test involved S. tapping as quickly as possible with a stylus upon a metal plate for a 10-second period. The number of taps was recorded on an automatic counting device. Two 10-second trials were given.

Seven S's were tested before and after the injection, the scores on each occasion of testing on the two trials being very consistent. The scores obtained under the two conditions and shown in Table II indicate that all the individuals tested became slower under the drug condition, the trend being significant at an acceptable level (t=2·090).

TABLE II

Tapping Speed

Subject	Non-Drug	Drug
1	98	82
2	111	87
3	118	92
4	104	93
5	112	74
6	113	103
7	81	79

The figures in the table represent the sum of the number of "taps" on two 10-second trials.

Spiral After-Effect

There is evidence which suggests that an organic condition may reduce the duration of the after-effect on the Archimedes Spiral (Holland and Beech, 1958). It has also been reported that barbiturates may reduce the duration of the after-effect (Eysenck, H. J., Holland, H. C., Trouton, D., 1957), and it was mainly for this last reason that the measure was employed.

Only three subjects were tested both before and after the drug; two other individuals could not be tested after taking the drug because of feelings of nausea. The three subjects tested were given two trials under each condition, the results being presented in Table III.

TABLE III

Spiral After-Effect

Subject	Drug Condition	Non-Drug Condition
1	0	23
2	6	21
3	32	46

The figures above refer to the total duration of the after-effects in seconds, on two trials.

It will be seen that all three S's showed decrement, and it seems reasonable to suggest that Sernyl probably has the same general effect as barbiturates where certain functions are concerned.

Critical Flicker Fusion

Critical flicker fusion thresholds are known to be sensitive to a wide range of influences, in particular the effect of barbiturates on this function is to reduce thresholds for the perception of fusion.

Seven of our S's were tested before and approximately 30 minutes after the administration of Sernyl, the thresholds under both conditions being established on "up" and "down" trials (i.e. from "flicker" to "fusion" and *vice versa*).

All S's tested in this way showed changes in the direction of lowered thresholds—i.e. required a lower rate of flicker in order to perceive fusion under the influence of Sernyl ($t=3\cdot868$). This change, as pointed out above, is in the same direction as that which is produced by the action of barbiturates.

Time Estimation

In this test S's were asked to estimate 10, 15 and 20 second intervals under drug and non-drug conditions. Each of 11 S's was given three trials on each time interval under both conditions.

The results presented in Table IV indicate a general trend for the S's to over-estimate the time intervals under non-drug conditions, and to under-estimate the intervals under the influence of Sernyl. Here, over-estimation

TABLE IV

Time Estimation

	Drug	Non-Drug
No. of over-estimations	11	24
No. of under-estimations	22	9

Table showing number of judgments falling into the categories "Over-estimation" and "Under-estimation" under the two conditions.

https://doi.org/10.1192/bjp.106.444.912 Published online by Cambridge University Press

refers to the tendency to judge that the interval has passed when, objectively, a longer time interval has elapsed; under-estimation refers to the tendency to judge a given time interval to have passed when, objectively, a shorter interval has elapsed.

A chi-square of 10·28 was obtained for the data presented in Table IV, indicating a real difference between the two conditions respecting time estimations.

Interesting trends were also noted respecting time estimation for those S's tested repeatedly following the administration of Sernyl. In Figure 2 these trends for one individual are reproduced, the three curves representing judgments of 10, 15 and 20 second intervals. These curves indicate a progressive degree of under-estimation up to 90 minutes after the injection, followed by a recovery period which, presumably, would have continued up to the average judgment for the non-drug condition had measurements been continued.

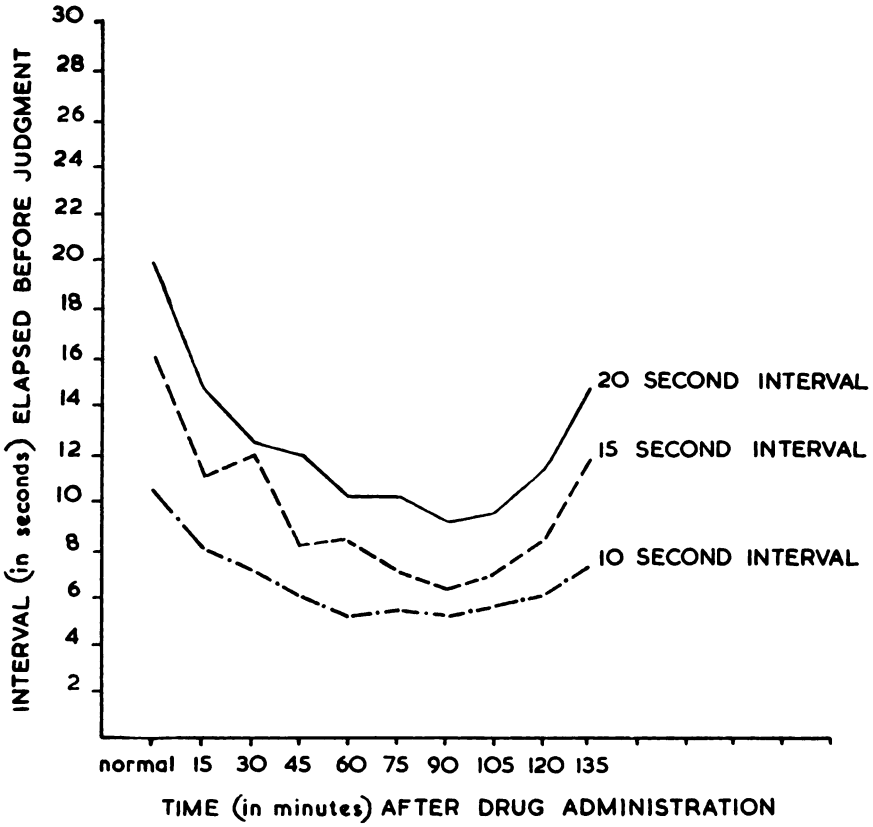

FIG. 2.—Individual time judgments at varying intervals after taking Sernyl.

Learning

It was of interest to examine the effects of Sernyl upon learning and recall, and to this effect two of our S's were tested using auditory paired associates.

Both S's experienced extreme difficulty in learning three "difficult" paired associates (e.g. Judge—Bowl), but had no trouble with "easy" pairs (e.g. Stop—Start).

Results obtained from one of our S's suggested that, in addition to producing a difficulty in learning new material, the drug might disrupt newly-formed associations. For this individual five pairs of numbers and letters were presented (e.g. M—6, S—2) and learned to a criterion of three correct reproductions.

This learning took place immediately before the injection, and recall of the material was obtained approximately 15 minutes after the injection. It was found that substantially more trials were required to reach the criterion during the recall period than during the initial learning, although one would ordinarily have expected the opposite to be true.

A further interesting point which emerged during the "recall" period in the S. referred to above was that some "incorrect" responses seemed to represent a recapitulation of "old" learning—e.g. the response "5" was repeatedly given to the stimulus letter "V" instead of the "correct" response of 7.

Proverbs

The test of the ability to state the meaning of proverbs was given partly in order to obtain a rough assessment as to loss in cognitive efficiency and partly because some authors believe that a schizophrenic disorder produces impaired ability correctly to define proverbs (Gorham, 1956).

The responses of individuals under Sernyl to Gorham's list of proverbs were extremely variable; all seemed to experience more difficulty in expressing their thoughts when under the drug and this difficulty was most marked in some cases.

In general it took much longer for a S. to explain the meaning of a proverb under Sernyl than in a normal state. Some responses obtained under the drug condition were extremely "concrete"—e.g. one individual's answer to the proverb "New brooms sweep clean" was "Of course new brooms sweep clean . . . they have longer bristles . . . old brooms are worn and don't make a good job of sweeping".

This degree of concreteness was, however, infrequent in our sample. Nevertheless, there was a tendency to produce answers of poorer quality under Sernyl than would ordinarily be expected from a sample of individuals all of whom were of high intelligence.

Conclusion

Although these findings must be regarded as essentially tentative, they suggest that certain interesting dysfunctions and changes in function appear under the influence of the drug used.

Some of the effects noted suggest that, on certain psychological tests, Sernyl acts in the same way as barbiturates. Other findings reported would indicate that the effects of this drug are not incompatible with effects produced by a schizophrenic process, although there is a decided lack of positive evidence for this drug as a schizophrenomimetic agent.

More systematic and detailed investigations of Sernyl are clearly indicated.

Discussion

There can be no doubt that Sernyl produces a syndrome of great interest to the psychiatrist and psychologist. Intravenously, in the dosage used, the acute effects begin at once (unlike LSD) and are over within an

hour. Though general malaise then persists for several hours, this relatively short period of disturbance is very convenient for the study of a model psychosis. Many of the symptoms and signs produced are similar to those that occur with other psychoticomimetic drugs and some of these have been contrasted in Table V. It will be seen that it is the absence of hallucinations that

TABLE V

Cardinal Symptoms and Signs Produced by Some Psychoticomimetic Drugs and Sensory Deprivations

	L.S.D. (Stoll, 1947)	Mescaline (Tayleur Stockings, 1940)	Hashish (Berringer, 1932)	Sernyl	Sensory Deprivation (Bexton *et al.*, 1954)
1. Onset of symptoms	Within ½-hour (Orally or I.V.)	Within ½-hour	2-3 hours	Immediate I.V. 1-2 hours orally	Variable
2. Prominent symptoms last	8 hours	10-12 hours	6-8 hours	1-2 hours	Up to 1 hour
3. Hallucinations:					
(*a*) Visual	+++	+++	+	+	++
(*b*) Auditory	++	++	+	0	0
(*c*) Somatic	+	++	+	+	+
(*d*) Tactile	0	0	+	0	+
4. Hyperacusis	++	++	+	++	++
5. Body image disturbances	++	++	++	+++	++
6. Depersonalization	+++	+++	++	+++	++
7. Disturbances in time appreciation	+++	+++	++	+++	++
8. Mood:					
(*a*) Euphoria	+++	++	+++	++	+
(*b*) Depression	++	++	+	0	++
(*c*) Fear	++	++	++	0	++
9. Behaviour:					
(*a*) Restlessness	+++	+++	+++	+	++
(*b*) Catatonia	+	++	+	+	0
10. Thought Processes:					
(*a*) Slowness and difficulty in concentrating	+++	+++	++	+++	+++
(*b*) Perseveration	+	+	+	+++	0
11. Delusions	++	++	++	+	+
12. Physical Signs:					
(*a*) Dry mouth and lips	+++	+++	+++	++	++
(*b*) Nausea	+++	+++	++	+	0
(*c*) Vomiting	++	++	++	+	0
(*d*) Tremors	+++	+++	+++	++	+
(*e*) Increased deep reflexes	+++	+++	+++	+++	+
(*f*) Nystagmus	0	0	++	+++	0
(*g*) Dilated pupils	+++	+++	+++	+++	0
(*h*) Diminished pain+temperature appreciation	++	+++	0/increased Sensitivity	+++	+
(*i*) Diminished proprioception	+++	+++	0	+++	+
(*j*) Respiratory changes	++	++	++	0	0
(*k*) Cardiovascular changes	+	+	++	0	0

KEY:
0=Does not occur. +=Occurs occasionally.
++=Often occurs. +++=Usually occurs.

is the main distinguishing point between the model psychosis produced by Sernyl and LSD and mescaline (though as Meyer *et al.*, 1959, report, at doses of more than 10 mg. hallucinations do occur). Luby *et al.* (1959) commenting on this, suggest that the symptoms produced by Sernyl and certain primary symptoms of schizophrenia, may have a similar basis, and suggest,

as a tentative hypothesis, that they may arise from a dysynchrony or defect in proprioceptive feedback mechanisms.

Consciousness is altered in the model psychoses, yet it is difficult to define this alteration. Mayer-Gross, Slater and Roth (1955) writing of the state of consciousness in mescaline intoxication, say, "It is difficult to classify the state of consciousness during the intoxication which allows of such full self-observation and, at times, seems to foster detachment and self-scrutiny. At other times, the same subject seems to have lost all clarity of consciousness, is drowsy and even close to sleep. The continuity of consciousness may be disrupted and fragmented. Single impressions are dissociated and without connection at one time, and, at another, everything seems to flow in a unified stream of deep significance and importance, related in some way with the whole past life of the subject, who identifies himself with it. The breadth and capacity of consciousness may also be changed, constricted to a single small impression, as when one subject said that for him, the whole world was contained in "a fluff of dark wool on the doctor's white coat". In the dosage used, Sernyl usually affects the clarity of consciousness, though often, there are brief episodes of clear consciousness. "Self-scrutiny" was described by three subjects, and the significance of small, everyday objects, by two. In general, there is nothing like "the extraordinary faculty for self-observation and introspection" that Stockings described with mescaline. This would appear to be another major difference between the model psychoses produced by Sernyl and mescaline. The differences between the experiences of a patient who received both LSD and Sernyl, are described in the following paper.

Meyer *et al.* (1959) believe that Sernyl produces a form of sensory deprivation and suggest that the drug acts primarily on the sensory cortex, brain stem and thalamus. They contrast this centrally mediated sensory deprivation syndrome with that produced by depriving subjects of all external stimuli (Bexton *et al.*, 1954). The symptoms produced by this latter technique vary considerably from one subject to another. The resemblances and differences between these syndromes need to be studied further before final conclusions can be made. It is noteworthy that schizophrenics are made worse by Sernyl (Luby *et al.*, 1959) yet they may be tolerant of external sensory deprivation; indeed, hallucinations are reduced in intensity in some patients (Harris, 1959).

This study has suggested that each aspect of the Sernyl experience should be systematically investigated, using objective measures, preferably in intelligent volunteers who have no psychiatric knowledge. Specific hypotheses should be formulated and then tested so that comparisons can be made between the effects of Sernyl and other drugs (particularly LSD and barbiturates); the effects of Sernyl and sensory deprivation; and the effects of Sernyl and the primary symptoms of schizophrenia. In view of the report by Luby *et al.* (1959) that chronic schizophrenics were made worse by the administration of Sernyl and that this deterioration persisted for some weeks, it would seem unwise to repeat this observation, though it might be considered justifiable to administer the drug to patients who have made a good recovery from a schizophrenic illness of short duration. The effects of suggestion in producing accessory symptoms (Abramson *et al.*, 1955) should be clearly defined and, if possible, these symptoms correlated with personality variables. The modification of the Sernyl experience by tranquillizing drugs is also an important subject for investigation as is the study

of other drugs of the cyclohexylamine series. Some of these investigations are now being made.

Summary

The drug Sernyl is described and the relevant literature reviewed. It was the first of a cyclohexylamine series introduced into anaesthetic practice because of its ability to produce analgesia without loss of consciousness. Post-operatively, however, psychiatric disturbances were common and the use of the drug in anaesthetic practice was curtailed. The drug appears to act at the thalamic level and produce changes in the reception of sensory stimuli. The effects on twelve normal volunteers are described and these contrasted with other psychoticomimetic drugs. As a result of this pilot study, possible lines of research are mentioned. As its action is relatively short, the syndrome produced is convenient to study from the psychological point of view.

Acknowledgments

We are very grateful to the volunteers who co-operated so well, even when asked to repeat tedious psychological tests under drug conditions, and to Dr. Linford Rees for his advice and encouragement. Sernyl was provided by Parke, Davis & Co.

References

1. Abramson, H. A., Jarvik, M. E., Levine, A., Kaufman, M. R., and Hirsch, M., *J. Psychol.*, 1955, **40**, 367.
2. Berringer, K., *Nervenarzt*, 1932, **5**, 346–357.
3. Bexton, W. H., Haron, W., and Scott, T. H., *Canad. J. Psychol.*, 1954, **8**, 70–76.
4. Eysenck, H. J., Holland, H. C., and Trouton, D., *J. Ment. Sci.*, 1957, **103**, 650–655.
5. Foulds, G. A., *Brit. J. Psychol.*, 1951, **42**, 209–217.
6. Gorham, D. R., *Clinical Manual for the Proverbs Test*, 1956. Waco, Texas: V.A. Centre; Baylor University.
7. Greiffenstein, F. E., De Vault, M., Yoshitake, J., Gajewski, J. E., *Anaesthesia and Analgesia*, 1958, **37**, 283–294.
8. Harris, A., *J. Ment. Sci.*, 1959, **105**, 235.
9. Holland, H. C., and Beech, H. R., *ibid.*, 1958, **104**, 466–471.
10. Huston, P. E., Shakow, D., and Riggs, L. A., *J. Gen. Psychol.*, 1937, **16**, 39–82.
11. Lear, E., Suntay, R., Pallin, I. M., and Chiron, A. E., *Anaesthesiology*, 1959, **20**, 330–335.
12. Luby, E. D., Cohen, B. D., Rosenbaum, G., and Gottlieb, J. S., *A.M.A. Arch. Neurol. Psychiat.*, 1959, **81**, 363–368.
13. *Iidem.* To be published.
14. Meyer, J. S., Greiffenstein, F. E., and De Vault, M., *J. Nerv. Ment. Dis.*, 1959, **129**, 54–61.
15. Nelson, E. H., "Experimental Investigation of Intellectual Speed and Power in Mental Disorder", 1953. (Unpublished Ph.D. Thesis, University of London.)
16. Mayer-Gross, W., Slater, E., and Roth, M., *Clinical Psychiatry*, 1955. London: Cassell & Co. Ltd., p. 363.
17. Shakow, D., and Huston, P. E., *J. Gen. Psychol.*, 1936, **15**, 63–104.
18. Stoll, W. A., *Schweiz. Arch. Neurol. Psychiat.*, 1947, **60**, 279–364.
19. Tayleur Stockings, G., *J. Ment. Sci.*, 1940, **84**, 29–47.