

PRELIMINARY INVESTIGATIONS OF THE EFFECTS OF SERNYL UPON COGNITIVE AND SENSORY PROCESSES

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IN a previous paper, Davies and Beech (4) presented data obtained from both clinical observations and psychological tests on normal subjects under the influence of Sernyl. In that paper an account was given of the chemical constitution and action of the drug. It is not necessary to say more here than that this compound is a synthetic cyclohexylamine derivative that was introduced into anaesthetic practice because of its ability to produce analgesia without loss of consciousness. It appears to act mainly at the thalamic level and produces changes in the reception of sensory stimuli. Post-operatively, however, psychiatric disturbances were common and the use of the drug in anaesthetic practice was curtailed. Our interest in Sernyl has centred upon its psychotomimetic effects and its possible mode of action. It has, in fact, been suggested that normal individuals under the influence of Sernyl behave, in some respects, like schizophrenic patients and that this similarity is most striking in the case of thinking processes. In the further investigation of the effects of this drug it was therefore decided to test the hypothesis that Sernyl produces mental disturbances which are characteristic of thought-disordered schizophrenics.

A second, and perhaps more far-reaching, aspect of the current investigation has been concerned with the action of Sernyl upon limiting sensory input. This line of enquiry seemed worth while, not only in terms of the observation made in our previous paper (4) that the drug seemed to alter auditory perception, but also in terms of the apparent link between reduction in type and amount of stimulation on the one hand and mental disturbance on the other.

MATERIAL AND METHODS

Subjects. Both aspects of the investigation were conducted using a sample of normal subjects. This sample comprised 21 individuals ranging in age from 20–50, covering a wide range of occupations. All these subjects were above average in intelligence and none of the subjects were acquainted with the nature of the drugs given nor of the purpose of the experiment.

Subjects were allocated randomly to either the Sernyl (experimental) group or to the Sodium Amytal (control) group, the test administrator being unaware of the drug group to which any individual had been allocated. Ten

subjects formed the Sodium Amytal group and eleven were allocated to the Sernyl group, the additional member of the latter group being necessary because of an error in the administration of the test of thought disorder for one experimental subject. For the auditory threshold test, therefore, the experimental group has an N of 11 while the control group has an N of 10; for the thought-disorder test both groups have an N of 10.

Dosage. All subjects were given the drug, whether Sodium Amytal or Sernyl, prior to the commencement of testing. In each case the drug was contained in an identical capsule. The dosage of Sernyl employed was 7.5 mg., while that of Sodium Amytal was 200 mg.

METHODS

1. *Thought Disorder.* It was decided to use the Bannister Test in this connection (1). In his thesis Bannister reported that several of his measures were capable of differentiating between thought-disordered schizophrenics on the one hand, and schizophrenics without thought disorder, normals, neurotics and depressives on the other. Such differentiation was maximized as a measure which he called "Consistency of Relationships" and for this reason only this score was used in our experiment.

For a detailed discussion of the test and its rationale the reader is referred to the original thesis (1), but some idea of the method might be obtained from the following description.

In the test the subject is asked to supply a list of 36 names of people who are known to him, and then is supplied with a list of ten characteristics such as "Good", "Lazy", "Religious", "Prejudiced". He is then asked to take 18 of the names given and divide these into two packs of nine according to each one of the labels—e.g., to divide his 18 names so that the nine "Lazy" people appear in one pile and the remaining nine are left in the other pile. This process is repeated for each of the remaining ideas or constructs.

Next the subject is asked to repeat this procedure, using the same ten constructs, but this time employing the second group of 18 people from the total of 36.

When the subject has completed this second sorting it becomes possible to examine the record of responses in order to see whether certain ideas or constructs go together. If, for example, all the people who are called "Good" by a subject are also called "Religious", then these two ideas would be strongly related for this subject. In general, normal individuals produce *consistent* results for the first 18 and second 18 people supplied by them—i.e., if "Good" and "Religious" are related on the first group of 18, then these two ideas are related on the second group of 18. Thought-disordered schizophrenics on the other hand, tend to show a *lack of consistency* in their usage of constructs and Bannister has employed a simple correlational procedure to indicate the degree of consistency on the two parts of the test.

In the experiment reported here we have compared the consistency of relationship scores for our Sernyl and Amytal groups with the normative data provided by Bannister for thought-disordered schizophrenics (N=8) and normals (N=20) not influenced by drugs.

The experimental procedure involved administration of the drug, either Sernyl or Sodium Amytal, following which the subject was questioned from time to time about his feelings. He was instructed to tell the experimenter as soon as he began to notice any alterations in his physical or psychological state,

but he was not told what drug had been administered, nor was he given any idea as to what experiences might be encountered. When such changes were reported (typically some $\frac{3}{4}$ hour after taking the drug) the Bannister Test was administered.

2. *Auditory Threshold Changes.* The procedure adopted here was to first test the patient's auditory thresholds on a standard Peter's audiometer before taking the drug, following which re-assessment of threshold took place between the first and second parts of the Bannister Test. The method adopted was to ascertain the threshold on one frequency only (1,000 c.p.s.) by giving ten ascending and ten descending trials, the average of these 20 trials being adopted as the "true" threshold.

The measure of change in audition involved subtracting the average value on the second occasion of testing from that obtained on the pre-drug trials. In the case of Sernyl, our prediction was that the threshold would be lowered after taking the drug, while in the case of Sodium Amytal, as a result of previous work, we predicted a rise in threshold.

RESULTS

1. *Thought Disorder.* Table I shows the results of comparing our two drug groups with Bannister's samples of thought-disordered schizophrenics and normals uninfluenced by drugs. It is clear from these data that our drug samples lie between the other two groups; neither Sernyl nor Sodium Amytal subjects produce scores significantly different from non-drug normals, but while Sernyl subjects are significantly differentiated from thought-disordered schizophrenics the Sodium Amytal subjects are not.

TABLE I

Significance of differences between Sodium Amytal, Sernyl, non-drug normals and thought-disordered schizophrenics on the measure Consistency of Relationships.

Groups Compared	<i>t</i>	Significance Level (1-tail tests)
Sernyl v. Sodium Amytal	0.551	N.S.
Sernyl v. Non-drug Normals	0.855	N.S.
Sernyl v. Thought-disordered Schizophrenics ..	1.804	p=0.05
Sodium Amytal v. Non-drug Normals	1.493	N.S.
Sodium Amytal v. Thought-disordered Schizophrenics	1.283	N.S.
Non-drug Normals v. Thought-disordered Schizophrenics	2.837	p=0.01

These subjects are somewhat equivocal, but they suggest that Sernyl does not, at least in the dosages administered in this experiment, produce effects like those found in thought-disordered schizophrenics. Furthermore, it would appear that on this test of thinking Sernyl has no greater disruptive effects than Sodium Amytal.

2. *Changes in Auditory Threshold.* The statistics in Table II show the results of comparing Sernyl (N=11) and Sodium Amytal (N=10) S's for auditory threshold changes.

TABLE II

Mean change in threshold from pre- to post-drug conditions

Sernyl	Sodium Amytal
-1.106	+0.940

Significance of difference between pre- and post-drug trials

Sernyl	t=1.258 (N.S.)
Sodium Amytal	t=1.498 (N.S.)

Significance of difference between threshold changes for Sernyl and Sodium Amytal groups

t=1.857 (p=0.05)

Although the changes in threshold for the two groups are in the predicted directions, Sernyl lowering and Sodium Amytal raising thresholds, in neither case does the trend achieve an acceptable level of significance. Our first two predictions are, therefore, not confirmed by these data. However, of eleven Sernyl subjects, seven manifest lowered thresholds on the post-drug trials, one remains the same, and two show rises in threshold. Of the ten Sodium Amytal subjects seven show rises in threshold while three manifest the opposite tendency. It would seem that these figures merit further investigation of changes in auditory perception in response to Sernyl.

Our third hypothesis, that the two drug groups would be significantly differentiated respecting their threshold change scores, is confirmed by these data.

DISCUSSION

The disruptive effects of certain drugs can usefully be likened to the action of psychotic processes and Sernyl is one of the most interesting of these chemical compounds. It is clearly necessary to investigate such effects and to examine their similarity to those produced by psychotic illnesses. By this means we may gain some knowledge of the mechanisms involved in psychotic processes.

We have, therefore, adopted an experimental procedure which sets out to answer two problems posed by the action of the drug Sernyl. The first of these problems has been concerned with the effects which Sernyl might have upon thought processes, and in particular whether this drug actually does produce a usage of constructs which appears to be characteristic of patients suffering from "schizophrenic thought disorder". This test which we adopted as a measure of this variable was one devised by Bannister, who was able to show, not only that the test differentiated between thought-disordered schizophrenics and other clinical groups, but between thought-disordered and non-thought-disordered schizophrenics.

The scores achieved by our two drug groups on this test fell somewhere between those obtained by thought-disordered schizophrenics and normals uninfluenced by drugs. While neither drug produced scores significantly different from those obtained by Bannister's normals, only the Sodium Amytal group could not be differentiated from thought-disordered schizophrenics. Our hypothesis that Sernyl produces effects in normals which are similar to those encountered in patients suffering from schizophrenic thought-disorder is therefore negated.

Our second problem has been concerned with beginning to explain some of the clearly disruptive effects of Sernyl by examining one kind of alteration in function produced by the drug. There is a body of evidence which points to a

relationship between certain abnormalities of functioning (such as hallucinations and disturbances in thinking) and reduction in the amount of available stimulation (2, 3, 4, 5, 7) and there is some evidence that certain mental disorders may, in fact, be "normalized" by exposure to such conditions (6).

It seemed to us at least possible that part of the effect of administering Sernyl could be attributed to the consequent alteration in the amount of available sensory input, and in our investigation we have tested one deduction from this thesis. Our prediction has been at this stage only concerned with one direct effect of the action of Sernyl—namely that this drug produces a measurable change in perception in one modality as a result of reducing sensory input in other modalities. Our predictions were not clearly confirmed in this experiment, but the results on the small groups employed certainly merit further investigation. If, on further investigation, we could produce clear-cut evidence for changes in auditory threshold after Sernyl, then it seems possible to set up the hypothesis that a number of the effects of this drug might be accounted for in the same terms, i.e., in terms of reduced sensory input.

One qualifying point should be mentioned. It may be that in the experiments described above, testing was conducted too soon after the administration of the drugs as Sernyl, in particular, produced maximal effects after about 1½ hours, and testing commenced approximately ¾ hour after taking the drug. Had we delayed testing until the full effects of the drug had been manifested, larger differences than those actually observed might have been obtained. It could also be argued that larger amounts of drug than those employed in this study might have increased the intensity of the effects and thus maximized the predicted differences. Clearly experiments which make good these faults are necessary and are, in fact, now being undertaken.

SUMMARY

Twenty subjects were given Sodium Amytal or Sernyl and the presence of thought disorder measured by Bannister's Test. The results ran counter to expectation, Sernyl subjects producing scores unlike those found in thought-disordered schizophrenics. In addition changes in auditory threshold were measured. The two drug groups were significantly differentiated by their threshold change scores. These results are discussed and further investigations suggested.

ACKNOWLEDGMENTS

We would like to express our gratitude to the volunteers for their co-operation and to Parke, Davis & Co., who provided the Sernyl and supported the investigation.

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