SOME FINDINGS IN THE AUTONOMIC NERVOUS SYSTEM IN SCHIZOPHRENIA*

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As in all areas of research into schizophrenia, the outstanding feature to date of work done on the autonomic nervous system in this condition has been the great variability of the findings. Low, normal, and high values of the measures used have been reported (Altschule, 1943), and this is true both of autonomic activity at rest and of responses to stress and drugs. The possible reasons for this are many. The sample of patients used has varied, and often the type of schizophrenic tested or the chronicity of the disease has not been recorded. The population used for comparison has often consisted of college students, and differences found may be due to the effects of hospitalization or a function of age. In earlier studies especially, the patients have been studied while on drugs, or insufficient time has been allowed to elapse between discontinuing medication and starting the tests. Often no measure of the patient's anxiety or emotional reactivity has been made, and differences found may have been due to this rather than the disease itself. There have been, too, many modifications of instrumentation and of drug dosage in different studies, with the result that overtly similar studies cannot be reliably compared.

In testing autonomic activity with drugs, seldom has any attempt been made to adjust the dosage on a weight basis, and the route of administration has varied even in the same experiment. If drugs are given by the intramuscular or subcutaneous route the rate of absorption will vary from patient to patient and, even in the same patient, at different times. Because of this, the difference in the response recorded would not be at all surprising.

Our aim has been, therefore, to measure several autonomically controlled variables: (1) at rest, (2) during stress, and (3) during response to drugs. Much has been written about the various autonomic variables and about what they actually measure (Darrow, 1943; Lacey, 1956) but we chose those generally considered as useful. Although many autonomic drugs have been used they fall into various groups: (1) sympathomimetic, (2) parasympathomimetic, (3) sympatholytic, and (4) parasympatholytic, and we have used examples from each group.

Sample

This study is part of the multidisciplinary investigation into schizophrenia, the chief object of which is to test, by applying a wide array of tests to a group of schizophrenics of mixed clinical diagnoses, the alternate hypotheses that schizophrenia is one disease or that it is many diseases. A further aim of this research has been to check tests previously reported as differentiating schizo-

phrenics from nonschizophrenics, and we have included, therefore, a control group of nonschizophrenics. Because the patients had to meet various criteria imposed by the different areas our sample is a specially selected one, but it included both acute and chronic patients and examples of the various clinical subgroups of schizophrenia. The patients were males, and their ages ranged from 18 to 50 with a mean of 35 years. There were 107 schizophrenics, 86 nonschizophrenics, and 14 of uncertain diagnosis. Before being tested they had all been off drugs for two months and, for a month prior to testing, had been on a strict diet.

Method

The tests were carried out over six recording sessions. Before the stress and drug experiments, the patient was familiarized with the procedure and with the surroundings of the test room. The environment was kept as constant as possible, the temperature 25 $\pm$ 1° C., humidity 40 per cent, the walls of the room were soundproofed, and there was a constant low, level background noise from the air conditioner.

At the end of the first session, recordings of all the measures were taken over a 5-min. period, and these were used as baseline values.

The next session was a stress experiment. After resting in the supine position and having had leads applied, a 5-min. baseline was recorded. The patient was then given a painful electric shock to his leg preceded at a 10-sec. interval by a tone every half minute for 5 min., and this was followed by a tone only every half minute for 5 min. A 15-min. recovery recording was then made.

The drugs were given over four sessions: (1) yohimbine hydrochloride, (2) piperoxan hydrochloride, (3) epinephrine hydrochloride and norepinephrine hydrochloride, and (4) mecholyl chloride and atropine sulphate. The last two sessions were carried out in another room and due to lack of time, records of blood pressure and EKG only were recorded.

All injections were given via a heparinized intravenous cannula inserted when the electrodes were applied. This Heyman-Olafson needle has a rubber diaphragm in it through which all the injections were given; thus it was possible to avoid upsetting the patient with the pain of an injection and to give accurately timed injections.

The drug tests began with a 5-min. baseline followed by the injection of saline and a 5-min. recovery recording. The active drug was then given slowly according to a strict schedule over 5 or 6 min., and a recovery recording was taken for a 15-min. period. If 2 drugs were given in one session, for example epinephrine and norepinephrine, an interval of 30 min. or more, if necessary, was allowed for return to baseline of the measures.

Drug dosage was adjusted to body weight as follows: yohimbine hydrochloride, 0.1 mg./kg./min., for 5 min.; piperoxan hydrochloride, 0.07 mg./kg./min., for 5 min.; epinephrine hydrochloride, 0.2 μg./kg./min., for 6 min.; norepinephrine hydrochloride, 0.2 μg./kg./min., over 6 min.; mecholyl chloride, 5 μg./kg./min., over 6 min.; and atropine sulphate, 8 μg./kg./min., over 5 min.

The recording instrument was a model T Offner EEG, and the variables

recorded were: (1) respiration: abdominal movements recorded by means of the change in resistance of a thin rubber tube filled with acetic acid; (2) EKG: taken from precordial leads to get records free from movement artifact; (3) ballistocardiogram: recorded during a highly damped system capable of a frequency response of 10/sec.; (4) skin temperature: taken by a thermistor fixed to the back of the fifth finger; (5) skin resistance: using a small alternating current to overcome the effects of polarization; and (6) blood pressure: recorded every half minute manually using a mercury sphygmomanometer.

The degree of anxiety or emotional reactivity of each subject was rated independently by 6 raters: 2 of them on the ward, 2 during psychological testing, and 2 in the polygraph room using a bipolar 8-point scale ranging from 0 (markedly under reactive) through 3 (normal) to 7 (greatly over reactive).

Results

For this analysis, a score for the resting activity of each autonomic variable was obtained for each subject by taking the mean value of the 5-min. resting baseline. The difference between this score and the mean of a fixed period during and after stress or a drug gave us a score for drug or stress responses.

The sample, for the purposes of comparison, was divided into five groups on the basis of psychiatric diagnosis as follows: (1) paranoid schizophrenics, (2) all other schizophrenics, (3) uncertain diagnosis, (4) nonschizophrenics with chronic brain syndrome, and (5) all other nonschizophrenics. An analysis of variance was carried out on these five groups.

A comparison of the resting autonomic activity of subjects showed only two statistically significant differences:

(1) The paranoid schizophrenic showed greater respiratory irregularity, both in depth and rate, than the others. This was at the 0.1 per cent level of probability.

(2) All the schizophrenics had a higher skin resistance at the 1 per cent level of probability.

In their response to stress we found no difference in the heart rate, blood pressure, or skin temperature change. However all the schizophrenics showed a greater fall in skin resistance than the other subjects. At the 0.1 per cent level of probability was the difference in respiration rate change during stress between the paranoids and the others.

Only one drug response seemed to differentiate the groups to any degree, the schizophrenic patient showing a smaller rise in blood pressure when given norepinephrine ($p < 0.01$).

A high degree of agreement was found between the six raters on the anxiety scale: $p < 0.005$. There was no significant difference in the anxiety score of our groups except for the paranoids, who had a slightly higher mean value.

Conclusions

Apart from those mentioned in the results, there seems to be no marked difference in the resting level of autonomic activity or its responsiveness to stress and drugs in the sample of schizophrenics that we have studied. The groups used in this analysis of variance have been similar in mean age and

in anxiety level. The subjects have all been hospitalized, off drugs for two months prior to testing, on a strict diet, and have been given the test drugs intravenously on a dosage-per-weight basis. The differences so often reported previously may have been due to one or more of these factors and not to the disease process itself.

However, it is true that although there was no difference in means, the variance in some of the measures was found to be much greater among the schizophrenics than among the nonschizophrenics. Therefore the next stage of our investigation will be, after finding the correlations between the autonomic variables and the biochemical, psychological, psychiatric, and social history areas of the Research Project, to find new meaningful subgroups within schizophrenia, using a combination of measures from these areas.

Acknowledgments

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