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PROGNOSTIC PREDICTION
OF THE INSULIN THERAPY
OF SCHIZOPHRENIA BASED
ON DATA ON THE HIGHER
NERVOUS ACTIVITY

TARTU 1964

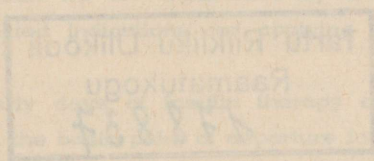


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Insulin therapy still occupies a leading position in the treatment of schizophrenia. It is regarded as the basic method for treating early schizophrenia. But clinical experience indicates that the efficacy of insulin treatment is by no means absolute. True, in quite a number of cases it is possible to achieve a greater measure of success by means of the prolonged and intense application of insulin treatment, and when progress is excessively tardy this may be combined with a supplementary convulsive treatment to produce more favourable results. Yet, in spite of all these combinations, there remains a certain number of patients in whom the application of insulin therapy does not produce more than a slight improvement. At the same time modern psychiatry disposes of other means which may obtain more effective results in patients who do not respond to insulin therapy. The task with which we are confronted is, therefore, that of attaining differentiated indications for applying various methods of treatment.

In the early days of insulin therapy clinical types were regarded as the basic point of departure for estimating the indications for treatment (M. Sakel 1935, M. Thumm 1938, A.G. Ivanov-Smolensky 1939, G.P. Popova-Pozen 1939, R. Elste 1940, etc.). Later on the main emphasis was transferred to more differentiated syndromes (M.J. Sereisky 1950, L. Bellak 1958, etc.), and in recent times even isolated psychopathological symptoms (H. Hoff, O.H. Arnold 1954, O.H. Arnold 1959, etc.). There is no doubt but that the general clinico-psychopathological data must con-

tinue to remain the basic criterion in selecting the type of treatment to be applied in each individual case. But clinical experience shows that the results of treatment may be widely different even in cases that are, from the clinical point of view, similar in every essential respect. This is evidently due to differences in the underlying pathophysiological mechanisms of the disease (V.V. Shostakovich 1958). Consequently a number of attempts have been made to estimate the prognosis of insulin therapy with a higher degree of accuracy on the basis of experimental investigation (e.g. the tests of Funkenstein, Rorschach and others).

In spite of the fact that we already possess abundant information on the manifestations of the higher nervous activity in schizophrenic patients, no noteworthy use has hitherto been made of this material to predict the results of treatment. Apart from a few references of a general nature (A.A. Kolessova 1955, J.E. Segal 1956), the only papers dealing with the subject in the extant literature are those of C. Astrup (1962-1963). Insufficient attention has also been paid to the criteria for long-term prognoses, with the result that the prophylaxis of relapsed cases does not always attain the requisite degree of accuracy. The clinical data used in estimating the immediate recovery following treatment (M.J. Sereisky 1939, N.P. Tatarenko 1950, 1958, A.I. Plotitcher 1958, 1959, 1961, A.V. Snezhnevsky 1962, etc.) need to be supplemented by objective experimental criteria, above all in the sphere of the higher nervous activity.

Investigations were carried out in the Tartu Psychiatric Clinic with object of estimating the prognostic criteria of insulin therapy. Both the higher nervous activity (association tests, the naming and grouping of pictures, tests of the motor reflex with speech reinforcement) and the vegetative functions (frequency of the pulse and breathing, the electrical resistance of the skin, the vegetative component of the orientation reflex)

were studied clinically and experimentally in 135 cases of schizophrenia examined dynamically before, during and after insulin treatment.

The duration and intensity of the treatment was determined separately in each individual case in accordance with the clinical dynamics of the patient. The immediate effect of the treatment was assessed on the five-point scale proposed by M.J.Sereisky (1939). Follow-up observations were continued for three to eight years after the conclusion of treatment, and the dynamics of remission were estimated throughout the whole period.

In all 43 functional signs were checked in each case (13 clinical and 30 experimental; 24 of the latter covering the higher nervous activity and 6 the vegetative functions). Using the summation method of N. A. Plokhinsky (1961) the reciprocal coefficients of linear correlation were calculated for all signs by electronic computer. Table 1 gives the correlations for the prognostically essential signs both before and after treatment. The coefficients may be regarded as statistically reliable from 0.28 onwards.

The statistical analysis of the data obtained makes it possible to draw certain conclusions.

Of the clinical characteristics, those which may be associated to a reasonable degree of accuracy with the quality of remission following insulin treatment are: the nature of the initial stage, the duration of the disease and the clinical syndrome.

In determining both the level of immediate recovery and the stability of remission after insulin treatment the most decisive factor to be taken into consideration is the duration of the disease. Analysis of the data shows that the efficacy of the treatment sharply diminishes after the passage of one year. The nature of the initial stage carries slightly less

PROGNOSTICALLY ESSENTIAL CORRELATION COEFFICIENTS OF
CLINICAL AND EXPERIMENTAL SIGNS IN 135 CASES
OF SCHIZOPHRENIA

| Functional sign | Condition before treatment | | | Condition after treatment | | |
|---|-----------------------------|-------------------------|----------------------|-----------------------------|-------------------------|----------------------|
| | Level of immediate recovery | Persistence of recovery | Prognosis of relapse | Level of immediate recovery | Persistence of recovery | Prognosis of relapse |
| Nature of initial stage | 0,60 | 0,34 | 0,36 | - | - | - |
| Duration of disease | 0,70 | 0,34 | 0,40 | - | - | - |
| Clinical type | 0,53 | 0,32 | 0,33 | - | - | - |
| Level of immediate recovery | - | - | - | - | 0,34 | 0,43 |
| <u>Association test</u> | | | | | | |
| Average difference in reaction time | -0,29 | -0,11 | -0,12 | -0,02 | -0,17 | 0,17 |
| Quality of responses | -0,29 | -0,24 | -0,17 | 0,36 | 0,34 | 0,36 |
| <u>Picture-grouping test</u> | | | | | | |
| Quality of responses | -0,11 | -0,23 | -0,12 | 0,33 | -0,13 | -0,12 |
| <u>Picture-naming test</u> | | | | | | |
| Median reaction time | -0,17 | -0,35 | -0,31 | 0,22 | 0,03 | 0,00 |
| Quality of responses | -0,14 | -0,31 | 0,00 | 0,30 | -0,10 | -0,03 |
| <u>Motor-reflex test</u> | | | | | | |
| Absence of old reflex | -0,27 | -0,28 | -0,28 | 0,21 | 0,08 | 0,17 |
| Absence of new reflex | 0,03 | -0,12 | -0,02 | 0,27 | 0,31 | 0,30 |
| Speed of formation of new reflex | 0,09 | -0,44 | 0,07 | -0,03 | -0,13 | -0,12 |
| Median reaction time | -0,07 | -0,28 | -0,23 | 0,23 | -0,10 | -0,10 |
| Force of motor reflex | -0,32 | -0,28 | -0,34 | 0,14 | -0,12 | -0,20 |
| Mobility of excitatory process | 0,15 | 0,20 | 0,25 | 0,36 | 0,24 | 0,28 |
| Differential inhibition | 0,34 | 0,31 | 0,40 | 0,20 | 0,32 | 0,35 |
| Conditional inhibition | 0,14 | 0,45 | 0,48 | 0,36 | 0,23 | 0,22 |
| Reporting back of relations in motor-reflex test | -0,12 | -0,12 | 0,03 | 0,36 | 0,37 | 0,31 |
| <u>Vegetative component of orientation reflex</u> | | | | | | |
| Complexity of vegetative component | 0,01 | -0,15 | -0,02 | 0,52 | 0,21 | 0,28 |

weight from the prognostical point of view, and a slow development at the onset may be taken as prognostic of subsequent deterioration. Least importance of all attaches to the clinical types of schizophrenia, though the efficacy of the treatment would appear to be somewhat smaller in the simple and hebephrenic types. The best and most stable remissions may be expected in incipient cases before differentiation, the degree of efficacy being only slightly less in the catatonic type. All the above-mentioned clinical factors are far more closely correlated with the level of immediate recovery than with the long-term prognosis.

A number of experimental signs possess reliable correlations with the characteristic signs of recovery, but their prognostic value is by no means equal. The stability of the old motor reflex, the force of the reflex, and the state of differential inhibition have points of relation both with immediate remission and with long-term prognosis. The reaction time in picture-naming and the state of conditional inhibition are connected with the long-term prognosis; but the quality of verbal responses and the average differences of reaction times in the association test are related only to the level of immediate recovery.

On the basis of these correlations, we may conclude that the presence of an extensive transmarginal (protective) inhibition of varying intensity in the higher nervous activity, coupled with slight disturbances of the internal inhibition, must be regarded as positive prognostic tokens. Slight transmarginal (pathologically inert) inhibition, coupled with profound disturbances of the internal inhibition point to the inadequacy and instability of the results of treatment.

On concluding the treatment, it often turns out that there is no parallel between the clinical effect and the experimental data for the nervous activity, but an analysis of the materials will make it possible for the investigator to determine

which experimental signs are most important in relation to both the real level of improvement achieved and to the long-term prognosis.

The clinical characteristics of recovery are closely interrelated: the higher the level of immediate remission, the greater the degree of its stability. But these correlations are not absolute. That is why it is particularly important to take into account the supplementary experimental criteria.

It appears that part of the experimental data typify both the real level of immediate remission and also the long-term prognosis (the quality of verbal responses, verbal reports of the relations in experiments with the motor reflex, stability of the new motor reflex). The remaining data (mobility of the excitatory process, the states of differential and conditional inhibition, complexity of the vegetative component in the orientation reflex) are correlated to only a few of the signs of recovery.

These correlations afford grounds for concluding that a marked diminution of transmarginal inhibition in the higher nervous activity, particularly in the second signaling system, should be regarded as the basic characteristic sign for the quality and stability of remission following insulin therapy. When the restoration of internal inhibition and mobility of the excitatory process is more or less complete, this may be interpreted as indicating a more optimistic long-term prognosis.

The results obtained may be taken as confirmation of the fact that the complex and dynamic investigation of the higher nervous activity by experimental methods will result in valuable supplementary information that may be used in estimating both short-term and long-term prognosis. In clinical practice we recommend a complex of experimental investigations involving simple methods which characterise the functions of the first and second signaling systems and their co-operation, as

well as cortico-vegetative relations. These may include association tests, picture-naming tests, picture-grouping-tests, motor reflex tests (with speech reinforcement and preliminary instructions), and investigation of the vegetative component of the orientation reflex. The data obtained from examination before treatment may be used to calculate the treatment with a greater degree of accuracy, thus supplementing the clinical data. The presence of transmarginal inhibition of varying intensity in both the first and second signaling systems, their co-operation and the cortico-vegetative relations, should be considered as an indication calling for the administration of insulin therapy.

Cases in which transmarginal inhibition of the higher nervous activity is weakly manifested, especially those in which the clinical symptoms are unfavourable, are best treated by a combination of different methods, or by psychotropic drugs. In such cases insulin therapy alone, no matter how intensive the treatment, does not produce decisive results, or may result only in a temporary improvement.

After conclusion of the treatment the data obtained from experimental investigation of the nervous activity make it possible to form a more accurate estimate of the real depth of remission and its long-term prognosis. A decrease in transmarginal inhibition in all the forms of nervous activity, accompanied by the restoration of internal inhibition, show that the effect obtained is positive and stable. In cases where the clinical remission is not yet complete, the so-called "after-maturity" phase may be expected to supervene.

On the other hand, in cases where clear signs of transmarginal inhibition persist after the conclusion of insulin treatment in the higher nervous activity, and especially in the second signaling system and the co-operation of the signaling systems, and where they are accompanied by pronounced distur-

bances of the internal inhibition, the results of treatment are superficial, in spite of the fact that the clinical remission may appear to be satisfactory. In such cases a sudden relapse may be anticipated and a complex after-treatment should be carefully applied.

The data presented testify eloquently to the fact that the experimental study of the higher nervous activity in schizophrenia is capable of making a valuable addition to both the theory of the disease and its practical treatment. These materials will enable the psychiatrist to use the most effective means at his disposal - insulin therapy - in a more purposeful way, and in so doing to contribute to a general increase in the efficacy of the treatment.

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