

# HUMAN BEHAVIOR AND GENETICS

EDITORS

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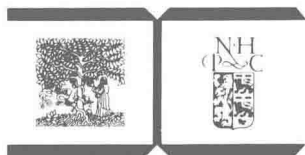
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*Editors*

WERNER SCHMID

*and*

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# HUMAN BEHAVIOR AND GENETICS

## PREFACE

This volume contains the papers contributed by speakers invited to participate in the Zurich Symposium on HUMAN BEHAVIOR AND GENETICS of the European Society of Human Genetics (ESHG) held at the University of Zurich, Switzerland, March 26-28, 1981.

During the last twenty years with the great progress in our science, meetings of medical geneticists have tended to deal mainly with physical aspects of inheritable disorders. Slowly, but steadily data have accumulated in human behavior genetics, and at the same time the medical geneticists have become aware of psychological problems inherent to the counselling process itself. Thus we thought the time had come to devote an entire ESHG Symposium to these mental aspects.

The major emphasis of the Symposium has been on behavior studies of children and adults with sex chromosome abnormalities; some of the papers clearly indicate that environmental factors such as, for instance, the degree of tolerance of society and of school systems play a very great role in the optimal mental development and the final achievements of these persons. Furthermore, it is important that professional counselling, information and, in some cases, hormone treatment are given at the appropriate ages.

Studies on behavioral patterns in patients with autosomal chromosome abnormalities have, so far, been relatively rare. The collected information is, however, interesting and it should provide a stimulus to future research. Psychological problems arising out of genetic counselling situations are dealt with in this volume in two very thought-evoking papers. Furthermore, we hope that the participation of psychiatrists with several papers indicates that the unfortunate gap between a part of the social scientists, psychiatrists and psychologists on the one hand and geneticists on the other hand is well on the way to be bridged.

Environment is of prime importance in human behavior. Many contributions in this volume show, however, the importance of studying the effect of genetic factors on mental development in order to be able to try to modify possible negative genetic effects by environmental-social factors.

Werner Schmid and Johannes Nielsen

We would like to express our gratitude to everybody who assisted in making this volume possible, not least the many secretaries for their part in the difficult job of preparing the camera-ready manuscripts.

Werner Schmid and Johannes Nielsen

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## INTRODUCTION

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When this symposium, dealing with aspects of "human behavior" was planned, more than three years ago, nobody - and certainly not the inhabitants of Zurich - were anticipating the behavior problems we have seen in our streets for the past nine months.

Compared to these large-scale violent outbursts of temper, observed in a not so small sector of - I think, genetically mostly normal - young people, in an affluent society, many of the problems of behavior in genetically handicapped persons may appear almost trivial - at least at a first glance.

The first glance, however, may convey a false impression. Common experience and history teach us that similar spells of bizarre behavior, riots and even outright revolutions have very limited durations. The hot heads cool down, and an age difference of very few years changes their minds and the behavior returns to what society deems acceptable.

On the other hand, behavior problems due to specific genetic causes such as gene mutations or chromosomal imbalance, whether they are mild or severe, as a rule pose a life-long problem, and one that will remain with us forever.

Many members of this Society have been actively and successfully involved in the discovery of new genetic entities. We have been fascinated by the still continuing progress in fields such as chromosome cytology and by the fact that we were witnesses of the elucidation of the causes of many strange clinical syndromes.

A great part of us share a similar professional evolution: specializing in one or the other field of medical genetics we became more and more involved in genetic counselling. In this process we made the experience that we are bound to know more than the laws of inheritance, more than cytogenetics, biochemical genetics or dysmorphology. In dealing with patients, parents and other persons seeking our advice, we are faced with duties and burdens which in most cases we

cannot simply hand over to a psychiatrist or a psychologist, unless we should have the exceptional chance of being a member of an ideal professional team.

One of our needs is more knowledge in respect to the long-term prognosis of the *mental* development of patients with specific genetic abnormalities. Furthermore, we want to know more about the optimal treatment and the possibilities of prevention of secondary deterioration. Also, we would like to know from therapists and educators, what they think we should improve in genetic counselling.

All these questions make it evident that this time the ESHG is holding an unusual meeting. We did not gather in first line to hear our favorite evergreens but we came to learn from experts, many of whom are not geneticists themselves.

Expertise in dealing with this group of patients is not evenly distributed among different countries of Europe, a fact of which many of us are painfully aware. While in some countries psychological research, therapeutic and educational efforts have - in this special field - reached a high standard, there is little awareness of the problems elsewhere.

A considerable part of the program is devoted to mental problems of patients with sex chromosome anomalies. This has two good reasons, a highly interesting scientific one and a socially important practical one.

From a scientific point of view the large groups of patients with XXY - Klinefelter's syndrome, the XYY men, the women with XO - Turner's syndrome and those with the Triplo-X condition, have a well delineated genetic disorder which is easily confirmed by a karyotype study. A considerable part of the patients exhibit problems affecting their personality and their relations with society. The greater part seems to be integrated quite well but still exhibits special traits of personality. The disturbances which we find in part of the XXY's and XYY's are, however, by no means limited to such patients but they are common among many chromosomally normal people. The difference is that in the latter we tend to believe that their troubles have diverse environmental as well as non-specific genetic causes. In the sex chromosome patients we know at least one main common genetic denominator in the members of the group. This provides the unusual opportunity to study the interaction of a given genetic constitution with the environment and this not in a remote field but in an area of psychology which is very close to the average spectrum of human behavior. Thus, we are faced with a unique opportunity to learn something in the nature-nurture problem.

The practical reasons which render the mental problems in sex chromosome

patients important in genetic counselling are the following:

1. What is to be done if one of these conditions is found for some reasons in a mentally so far normal young patient. Can or must we do something of preventive nature?

2. What is the optimal treatment if the patient already is mentally or socially deviant?

3. What is the balanced and objective information we can give to couples if one of these anomalies is discovered in second trimester prenatal diagnosis?

What we are hoping to learn is the experience of careful, unbiased and, if possible, long term observations.

Point two, the therapeutic approach is of great importance in our contacts with authorities in the health and jurisdictional sector. If there are observations pointing to a successful treatment of grossly asocial and criminal patients in these groups, ways must be found that this kind of treatment can be applied. My personal observations on what happened to some of these cases in Switzerland are appalling. A Klinefelter patient is serving one sentence after the other, committing the next crime, habitually in drunken state, on the first day after release; among other offenses, he has already committed a case of manslaughter. No attempts of therapy were made so far. A young boy with the XYY condition became very troublesome from the age of about 4 years. His mother had to transfer him from one school to the other, later from one institution to the next; with about twelve he began to set fire when things did not go according to his will. At the time I saw him, at the age of fourteen, he had to be kept under constant surveillance in the ward of a big mental hospital, together with all the incoming adult cases of acute psychoses etc. Although of practically normal intelligence this boy was so difficult to manage that no home for juveniles was ready to accept him any longer. I tried to draw the attention of numerous psychiatrists to this special patient with his dark social prognosis, but I had no success. I suspect that, among other reasons, nobody felt competent.

In this context, I must point out the particular situation in Switzerland. Health, education, jurisdiction and many other things are domains of our cantons or even communities and not of the federal government. While this extreme decentralization in general functions very well and even is the essence of the Swiss type of democracy, it has disadvantages in areas such as institutions for special types of the mentally ill and special penal institutions. Sometimes a number of cantons form what we call a concordate and create a common rehabili-

tation center or a special type of prison etc., but all this takes much longer and is bound to be less perfect than in some western countries with a strong central government. I know that we share our shortcomings with other European countries and our Danish and British experts can be sure of a very attentive audience.

The second part of our Symposium will be devoted to a wide variety of different topics, all of them, however, centered around the theme of mental problems in genetic disease and to other psychological points of special interest to the genetic counsellor. I think that we can look forward to a highly stimulating meeting.

## ADDRESS BY THE HONORARY PRESIDENT OF THE SYMPOSIUM

### HUMAN BEHAVIOR AND GENETIC RESEARCH, VIEWS OF A PSYCHIATRIST

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For the last 60 years I have followed with close attention what progress in genetics has meant for psychology and psychiatry. I shall try to give a short survey of this relationship as seen by a clinical psychiatrist.

*When I was a college boy*, Gregor MENDEL's laws had just been rediscovered. In Zurich, LANG and STANDFUSS were pioneers in research on Mendelian heredity. STANDFUSS allowed me to watch his crossing experiments. Mendelian heredity became my first great fascination in biology.

*When I was a medical student*, I was dreaming of participating in research with the aim of delineating the influence of Mendelian heredity and of life experience for every psychiatric disease entity in KRAEPELIN's system.

What was the situation with which I was confronted *40 years later*? The knowledge of MENDEL's laws had helped essentially in the understanding of many cerebral and metabolic diseases exhibiting psychopathological symptoms. In 1959 the first chromosomal anomaly was discovered and others followed soon later.

All these great discoveries concerned, however, diseases on the borderline between psychiatry, neurology and internal medicine, diseases which are relatively rarely seen in psychiatric practice with adults. But what about genetic research with regard to normal personality development and the mental disturbances the psychiatrist has to deal with in regard to neurotic personality developments, with regard to schizophrenic psychoses? In this respect the situation was far from satisfactory, it even seemed hopeless to many of us.

*Forty years after having started research*, I was faced with a large number of data collected during my endeavours to remain faithful to my early interests, data on the families of 627 schizophrenic patients of mine, on 1117 of their fathers and mothers, on their 2408 siblings and on over 5000 of their other relatives. As a means of comparison I had studied the families of 200 patients with somatic disorders and of a 100 alcoholics. I had also collected pedigrees

of schizophrenics reaching back two centuries and I had done family studies with the RORSCHACH test. I had constantly followed the literature.

My juvenile hopes to find simple Mendelian ratios were disappointed like those of most psychiatrists. The research on families of mental patients produced interesting results in other respects but the results as regards heredity were modest. They permitted the statement that normal and morbid personality developments - and also the development of schizophrenic psychoses - were due to the interaction between inborn dispositions and environmental influences - a vague statement which does not mean very much. The family studies had at least allowed the determination of empirical morbidity risks of the relatives of many mental patients, a result which is of practical use.

Confronted with these modest results, genetic research became uninteresting to many psychiatrists - and psychiatry to many genetists.

*Was such resignation justified?* Had genetic research in psychiatry come to an end?

*It has not!* Quite on the contrary, fascinating new knowledge opens the door for new research.

I shall mention a few new research results which are decisive for future genetic research in psychology and psychiatry:

1. We have learnt that the disease entities of classical psychiatry have not much to do with genetic entities. The prejudice towards the decisive significance of psychological diagnosis for evaluation of a genetic background is overcome.

2. We have learnt from psychological research that an equilibrium, a harmony of inner life (of interests, trends, impulses, moods and inclinations) is decisive for the healthy personality development - and the lack of such a harmony is decisive for developments towards a neurotic personality or a schizophrenic psychosis.

3. We have also learnt to distinguish between a biologically rooted basic psychic life and the truly human psychodynamic life. To the basic life belong:

- the degree of awareness, the trend towards activity or passivity, primitive moods
- primitive drives like thirst, hunger and satiety, tendency to aggression or submission, to explore or not to explore, sexual drives and many others
- basic psychological phases such as the 24-hours cycle, the menstrual cycles and newly discovered other cycles.

On the basis of this biologically rooted psychic life develops the human

psychodynamic life, the spiritual, intellectual, artistic life and the unique human affectivity.

4. Harmony or dysharmony in both psychic spheres are important for the personal development, but the basic psychic life is much more directly connected with heredity than the human psychodynamic life. It is particularly suitable for genetic research as it is possible to delineate within this basic psychic life particular, single tendencies, while in psychodynamic life every tendency is much more dependent on every other tendency.

5. Modern biochemical research enables us to study the basic psychic life in its relationship to neuroendocrine functions. The neuroendocrine system was acknowledged as a third part of the nervous system. It contains the endocrine neurons of the brain and the endocrine APUD cells in other organs (the amino-precursor-uptake-decarboxylation cells) and their receptor systems. The function of the neuroendocrine system comprises relationships between arousal, moods, drives, cycles, in short, between any component of the basic psychic life with humoral functions, in particular with the activity of peptide hormones.

*Surveying all these research results* we are able to draw conclusions for future genetic research on normal and morbid human behavior: The whole personality and an entire psychopathologic syndrome can hardly be the prime object of genetic research as they are the consequence of an integration of all inherited and all acquired influences on the psychic life, as they depend on the harmony or dysharmony of all these influences. More promising objects for genetic studies on human behavior are particular functions of the biologically rooted psychic life in their interaction with neuroendocrine functions.

All this may sound highly hypothetical but - as a matter of fact - *successful research* on the basis of these conclusions is already going on. I mention just a few examples:

- As a pioneer in this field DIETHELM in New York demonstrated the specific interrelationship between bradykinine (and other peptides) with particular moods.
- G. SMITH in New York studied the interaction between cholecystokinin, chewing food and satiety.
- In Zurich we studied the influence of clinically diagnosed hereditary endocrine peculiarities on the course of schizophrenic psychoses and of normal development.
- Abnormal phases of hormonal secretion have been shown to be important in

the understanding of Anorexia nervosa.

- The effect of androgens in the fetus and the equilibrium between heterosexual and homosexual trends is being studied.
- In Zurich, FISCHER and BLUM have opened a new way for investigating altered human behavior due to altered function of the parathyroid, showing that the parathyroid is influenced by dopamine and adrenaline.
- It has become probable that the blood platelets belong to the endocrine system, that their content of monoaminooxydase is genetically influenced and has much to do with changes in mood.

#### SUMMARY

Genetic research on the biological roots of psychic life is more promising than genetic research on the whole personality and on psychopathological syndromes.

For the new generation a new door has been opened for research on genetics of human behavior.



THE PATIENT WITH A CHROMOSOMAL DISORDER, THE PARENTS AND THE PROFESSIONAL TEAM. (Reactions from the parents of children with Down's syndrome).

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## INTRODUCTION

This year's meeting of the European Society of Human Genetics is specially devoted to behavioural, social and psychological problems concerning a number of genetic diseases including the chromosomal aberrations. Human cytogenetics are, as Vogel and Motulsky have expressed it, "successful late-comers in the field of human genetics" (1). The main achievements of human cytogenetics have been first the determination of the chromosome number of man, then the diagnosis and description of chromosomal syndromes with landmarks such as Down syndrome, sex chromosome aberrations and breakage syndromes and finally prenatal diagnosis with all its implications. These achievements have brought human genetics into close contact with society. The lay-man inevitably connects human genetics with chromosomes.

The findings of a serious chromosome aberration in an infant, child, or an adolescent will often change the life of the parents. Special demands are presented to counsellors, who have to face giving the diagnosis, the "bad news", to the family. The family goes through a situation typical of a crisis. Feelings of uncertainty, anxiety, depression, guilt, aggression and hostility, well known to psychiatrists and psychologists in crisis situations, are often found in parents after they have received information about a severe chromosomal aberration in their child (2).

When a chromosomal disease is suspected, a number of persons around the patient are involved in influencing the situation: The clinician, who may be an obstetrician, a pediatrician or a general practitioner, the cytogeneticist and the child psychologist are