GENE INTERACTION IN THE PHENOTYPIC EXPRESSION OF MENTAL DISEASES

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A genealogical analysis is carried out on the pedigrees of 10 twin pairs with two or more psychoses. The probands' symptoms reveal some peculiar aspects, i.e., an atypical phenomenology possibly due to the interference of more pathological genes. Schizophrenia, depression, epilepsy, and obsessive neurosis, are found in the pedigrees in different combinations. The study of these pedigrees would lead to the conclusion that interaction of more than one psychosis gives rise to atypical forms as a result of an attempt to establish a state of balance between opposing dynamic actions, as in reversible chemical reactions. Probands' symptoms are less severe and with an often more favourable prognosis. Epilepsy tends to become independent and the major psychoses seem to be epistatic on it. Af for obsessive-compulsive neurosis, probands may progress into schizophrenia or depression if one of these psychoses is present n the pedigree, or may represent the neurotic form of the major disease.

INTRODUCTION

The investigation of complex psychopathological manifestations, labelled as " Atypical Psychoses ", finds useful research tools in the twin method and in the study of pedigrees. They enable us to discriminate hereditary from environmental components and may lead to a better diagnosis, a selective therapy and a more reliable prognosis.

The genetical approach becomes a complement of the clinical investigation whenever some doubt in the classification and etiology of mental disease is aroused. Atypical psychoses do not follow entirely the symptomatology and course of the classical types but show characteristics which recall different forms or have intermediate symptoms.

The atypical varieties also include " mixed psychoses ". Mayer-Gross in 1932 included among these the cycloschizophrenic and the cyclo-epileptic combinations. Challiol (1942) summarized the possibilities of different intrapsychotic interferences. In 1950 Kleist and Schwab isolated the schizophrenic nucleus from the " systemic schizophrenies " (with a favorable outcome) and from " degenerative forms " (*Randpsychosen*) which include manic-depressive, paranoic and epileptic features. Leonhard (1960) on this ground considers atypic schizophrenia the disease which has a periodic course and a favorable prognosis. Sahli (1959) accepts the possibility of schizocyclic mixed psychoses, although he believes them to be uncommon. Kretschmer (1955) supports the hypothesis of mixed psychoses being due to constitutional pathoplastic factors. Mitsuda (1967) believes in the existence of mixed psychoses but considers the atypical forms as a genetic entity pertaining to the group of " peripheral " psychoses and, therefore, connected with schizophrenia, manic-depression and epilepsy.

The same uncertainty is found when speaking of atypical varieties of manic-depressive psychosis associated with schizophrenia (Pauleikoff 1957) or epilepsy (Mitsuda). Zerbin-Rudin (1971), in an overall critical review of the more recent opinions in the field of psychoses, states that the atypical forms are " undoubtedly genetically heterogeneous " and that an interaction between the different psychoses is to be expected when superpositions of symptoms are found in the pedigree.

CODEN: AGMGAK 25 240 (1976) — ISSN: 0001-5660
Acta Genet. Med. Gemellol. (Roma) 25: 240-243

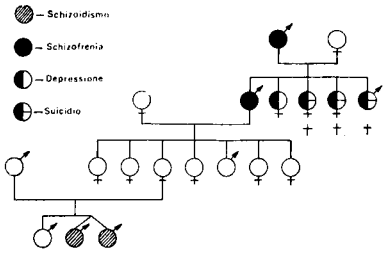
We will not discuss extensively the relationship between neuroses and psychoses; we will only point out what can be referred to obsessive-compulsive neurosis, in which cases with " a schizophrenic hue " (Bazzi and Matarazzo 1950, Lo Cascio 1954, Pauleikoff 1957) or with a depressive or epileptic background (Reda and Paretti 1958, Sakai 1967) have been described. The evolution and prognosis of these neuroses is often connected to psychotic components in the pedigree (Rosenberg 1968). We believe that a number of both genetical and environmental factors interfere in the moulding of a psychic phenotype. The atypical forms are due to complex genotypical trends which exert their influence modifying the expression of the disease in a sort of balanced symptoms. Although this balance may be unstable and pathological, nevertheless it helps to mantain an adaptability of the subject to his own social and cultural environment.

Assuming that different genes influence the same function through different channels acting in synergism or antagonism, the great plasmability, variability and reversibility of psychic reactions can be explained. The shock-therapies empirically exploit this antagonism to improve a typical psychosis; one can suppose that in atypical forms this may happen spontaneously and thus explain some cases with a more diluted symptomatology and a better prognosis.

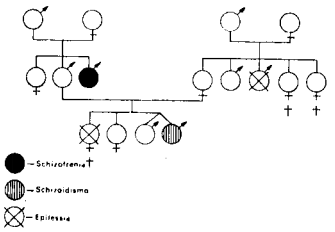
The present paper concerns some of these events in pedigrees of twins in which different pathologies are present and in which the probands show atypical symptomatologies that can be explained if observed from a genetical point of view.

The pedigrees of 5 MZ and 5 same-sexed DZ twin pairs followed over a number of years are presented in the following.

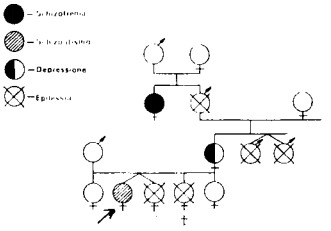
CASE REPORTS



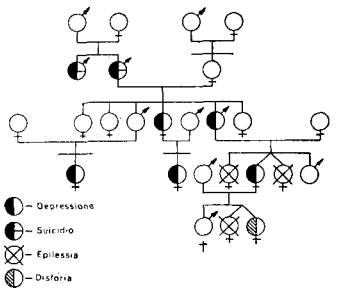
Case 1: *Schizophrenia and Depression.* MZ male 18 y.: Schizoidism. Great-grandfather with an unknown chronic psychosis. Grandfather with delusional schizophrenic behavior, one sister depressed, three siblings suicide. Parents free from mental symptoms. Probands show behavioural disturbances with poor interests, undirected restlessness of the schizoid type.



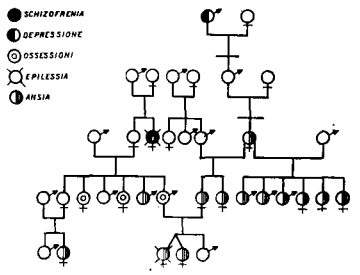
Case 2: *Schizophrenia and Epilepsy.* DZ male pair, 15 y.: Schizoid behavior. Paternal uncle schizophrenic; maternal one, epileptic. The proband shows a reactive, impulsive behaviour, dulling of affectivity, withdrawal of interests. Cotwin is healthy. One sister epileptic.



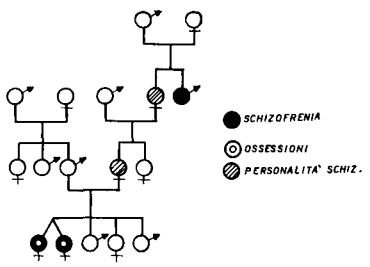
Case 3: *Schizophrenia, Depression, and Epilepsy.* DZ female pair, 17 y.: Delusional state. Maternal grandfather epileptic with a schizophrenic sister. Two uncles (MZ twins) epileptic. Mother with episodic depressive phases. One sister and the cotwin epileptic. The proband holds responsible for his failure parents and teachers; he isolates from people, with periods of apathy or reactive depression.



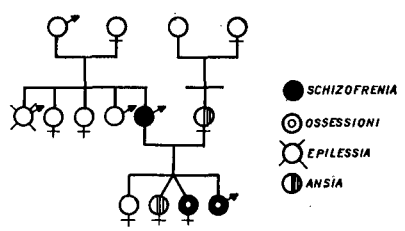
Case 4: *Depression and Epilepsy.* DZ female pair, 37 y.: Reactive depression. Great-grandfather and his brother committed suicide; grandfather and a sister had cyclic depression. Two mother's cousins suffered from depressive episodes; the mother (DZ twin) has depression. Cotwin and a sister epileptic. The proband shows a depressive state with anxiety and her cotwin is epileptic.



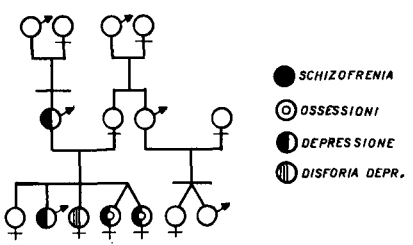
Case 5: *Depression, Schizophrenia, and Epilepsy.* MZ female pair, 15 y.: Enuresis, anxiety. In maternal and paternal pedigrees there is a spread of psychotic and neurotic diseases which seems to dilute in the probands, one enuretic and the other anxious.



Case 6: *Obsessive-Compulsive States and Schizophrenia.* MZ female pair, 30 y.: Schizophrenia. Grandmother's brother schizophrenic; grandmother with delusional mystic behaviour. Mother with hypochondriac personality. Both twins started at 15 with obsessive cerimonials which ended at 25 with a schizophrenic state, paranoid type, with some stereotypes without compulsion and insight.

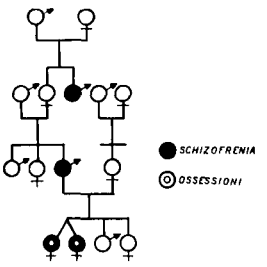


Case 7: *Obsessive State and Schizophrenia.* DZ female pair, 22 y.: Schizoid behavior. One uncle epileptic. Father schizophrenic. Mother with an anxiety neurosis. One brother rupophobic with schizoid behaviour. The cotwin is slightly anxious but free from mental symptoms. The proband started at 12 with compulsive trends and at 20 developed a schizoid behaviour with jealousy toward her cotwin, carelessness, apathy, poor insight.

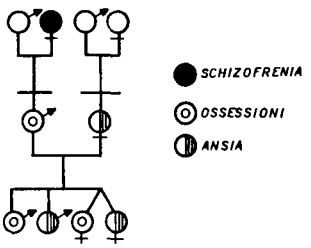


Case 8: *Obsessive State with Depressive Evolution.* MZ female pair, 26 y.: Depressive State. Father with depressive episodes. One brother depressed. One sister with mild depression. At 17 the twins develop compulsive behaviour with iteration, anxiety and self-criticism. At 26 there is a remission of compulsions and both enter a state of depression with ideas of suicide, ruin, and so on.

https://doi.org/10.1017/S0001566000014197 Published online by Cambridge University Press



Case 9: *Obsessive Neurosis with Schizoid Evolution and Alcoholism.* MZ female pair, 21 y.: Schizoid behavior. Grandmother's brother schizophrenic, paranoid type, with alcoholism. Father with paranoid schizophrenia. The second born twin starts at 10 with obsessive compulsions followed, at 15, by her cotwin. At 19, in order to relieve anxiety, the latter indulges in alcohol; at 21 she thinks that people observes her, becomes suspicious and isolates. The second born shows at 20 a delusional state (believes herself ugly, wants to be operated from a prominent chin, stands long hours in front of the mirror).



Case 10: *Obsessive Behavior.* DZ female pair, 20 y.: Compulsive neurosis. Grandmother schizophrenic, paranoid type. Father overconscious, rigid, tyrant. Mother anxious. The first born starts at 14 with obsessive ceremonials and at 20 the symptoms are still unchanged. The cotwin is only slightly anxious. An interesting feature of this family is that each twin repeats, years after, the symptoms of the elder brothers: one obsessive, the other anxious.

DISCUSSION

The cases we presented certainly do not allow any generalization concerning some peculiar expressions of mental disorders. The twin method selects some pathoplastic factors, which are more evident in same-sexed DZ pairs, but does not explain how the different genic actions produce the phenotypic picture. Nevertheless some deductions can be inferred:

1. The atypical forms of psychoses can coexist with mixed forms resulting from an interaction of genes which, if acting independently, give rise to specific symptoms (schizophrenia, M.D. psychosis, epilepsy in their typical varieties).
2. The association of two or more pathological genes develops atypical pictures having often a milder sympomatology and a more favourable prognosis.
3. Some types of expressions, classified as neuroses, may result to be microforms of a major psychosis, or may develop into it when exogenous or endogenous individual factors add their weight to the genetical ones.

REFERENCES

Bazzi T., Matarazzo F. 1950. Valore diagnostico e significato clinico-nosografico delle sindromi di tipo ossessivo-fobico della schizofrenia. Rass. Neuropsich., 4: 119.

Challiol V. 1942. Contributo allo studio delle psicosi miste. Arch. Psic. Neur., 1: 20.

Kleist K., Schwab H. 1950. Der denkverwritten Schizophrenien. Arch. Psychiat., 184: 28.

Kretschmer E. 1955. Korperbau und Charakter. Berlin: Springer.

Leonhard K. 1960. Die atypischen Psychosen und Kleist's Lehre von den endogenen Psychosen. In Grühle H.: Psychiatrie der Gegenwart [Bd. II].

Lo Cascio G. 1954. Nuove vedute sui confini tra psicastenia e schizofrenia. Lav. Neurop. 3: 246.

Mitsuda H. 1967. Clinical Genetics in Psychiatry. Kyoto: Bunko-sha Co.

Pauleikoffff B. 1957. Atypischen Psychosen. Basel: Karger.

Reda G., Paretti E. 1958. Stati ossessivi periodici nel quadro della psicosi depressiva. Riv. Sper. Fen., 82: 7.

Rosenberg C.M. 1968. Obsessional neurosis. Aust. N. Z. J. Psychiatry, 2: 32.

Sahli H.L. 1959. Übergänge manischer-depressive und schizophrener svrläufer. Psych. Neur., 138: 98.

Sakai T. 1967. Clinico-genetic study on obsessive-compulsive neurosis. In Mitsuda 1967.

Zerbin-Rüdin E. 1971. Genetische Aspekte der endogenen Psychosen. Fortschr. Neurol. Psychiatr., 39: 9.

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