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The Ergon/Chronon System in Schizophrenia

A Twin Study

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SUMMARY

Ten (eight MM and two FF) MZ twin pairs, with one or both schizophrenic members, have been examined. The disease was concordant in four pairs, discordant in one pair, and partly concordant in five pairs.

The time of onset was simultaneous in five pairs, but showed differences of three years in two pairs, and of one-two years in two more pairs. Concordance in the time of onset was not related to severity of the disease.

Is schizophrenia a genetic disease? Theories of aetiology of schizophrenia have antithetic poles — from primary organic atypicality versus familial and environmental causation, to interaction of the two factors dychotomy (process syndrome and reactive form) of them.

The family and twin methods converge to assign a primary role to genetic factors.

In the field of twin researches, where discrepancies are also evident, we studied one factor bound to the biology of the gene, i.e., the Ergon/Chronon System (Gedda and Brenci, 1969).

Ergon is the energy of information that ensures the degree of stability of the action and specificity of a gene. *Chronon* is the span of activity of a gene for a given function, i.e., the temporal dimension of a gene.

Ergon and chronon are variable dimensions following a stable general biological pattern, which may be modified by hereditary mutants or by environmental events.

Sample and Methodology

The study was based on 10 pairs of MZ twins (8 MM, 2 FF), aged 20 to 40, in which one or both cotwins manifested schizophrenic symptoms.

The propositi were observed in the Mendel Institute, often before the phenomenological expression of the disease, during its course, throughout eventual admission in Psychiatric Hospitals, and further until December 1970. The young age of the subjects does not allow to ascertain the outcome.

Zygosity was determined by anamnestic information, routine screening (blood groups, physical traits, EEG, etc.), so that doubts could be reduced to a minimum.

General examination and laboratory investigations were performed by physicians and specialists of the Institute in order to exclude any physical ailment which could interfere with mental symptoms.

The diagnosis of schizophrenia and its type was made on the basis of initial symptoms, course and evolution of the disease and confirmed by hospital records, when admitted.

Classification was included in the four main varieties: paranoid, catatonic, hebephrenic, and simple. Features of the varieties are grounded, respectively: (1) on persecutory delusional and dereistic thought with hallucination; (2) on phases of stupor and excitement in both of which negativism and automatism are preminent; (3) on loss of interests, autism, delusional ideas with religious, sexual, or social content; (4) on gradual change of personality, progressive inadequacy of school records, irritability, childishness of emotions.

Specific intelligence (Raven, Wechsler, etc.) and personality (Rorschach) tests were performed when possible.

Family histories were taken from one or both parents who were directly or indirectly examined through a series of individual interviews.

Results

Results (see Table) can be summarized under three items: (1) familiarity (heredity); (2) specificity, stability, and severity of symptoms (ergon); (3) onset and course (chronon).

FAMILIARITY. In five pedigrees (cases 1, 5, 6, 9, and 10), there has been a case of schizophrenia among relatives of second degree (cousins, uncles or aunts, grandparents). None among parents and siblings.

In four pedigrees (cases 4, 5, 7, and 8), there has been severe neurotic behavior (7, 8), nonspecified psychosis (7), depressive and delusional cases with suicide (5), alchoolism (4).

In two pedigrees no mental diseases have been reported or elicited during interviews. Three of the four severe cases had a schizophrenic relative.

Schizophrenia — as far as our sample is concerned — runs in five families; psychotic or severe neurotic behavior, in three. *The disease has a genetic linkage which manifests itself with recessive transmission* and which may be tied to other affective illnesses.

TYPE OF SYMPTOMS, SPECIFICITY, SEVERITY, AND STABILITY (ERGON). Nine pairs, among the ten examined, were concordant in their symptoms; one pair was discordant; one paranoid, two catatonic, three hebephrenic, and four simple cases of schizophrenia have been diagnosed.

All nine concordant pairs had the same symptoms, even when dyschronia was present (cases 2, 4, 6, and 8). Different degree of expression was always on the ground of same type of behavior. Rorschach test showed the same basic personality disturbances (stereotypy, rigidity, negativism, poor interest, emotional coartation). In the discordant pair the healthy subject revealed, too, in the Rorschach test, poor emotional charge, hostility, suspiciousness, poor abstraction, futility.

Schizophrenia is a baffling multifaced disease and its semeiology is still a puzzling

Table. Analysis of schizophrenia in ten MZ twin pairs

Case no.	Birth date	Sex	Diagnosis	Onset			Severity concordance			Heredity			Extragenetic factors	Course (1970)
				Date	Age	Differ.	Total	Partial	None	Spec.	Aspec.	None		
1	1932	MM	Paran. Paran.	1965 1965	23 23	—	Severe			+			— —	Defect Defect
2	1941	MM	Catat. Catat.	1960 1958	19 17	2	Severe					+	— —	Pseudodepr. Pseudodepr.
3	1941	MM	Hebephr. Hebephr.	1959 1959	18 18	—	Mild					+	— —	Under treat. Under treat.
4	1943	MM	Simple Simple	1961 1962	19 19	—		Mild Borderl.			+		Enteritis in infancy —	Defect Unchanged
5	1944	MM	Simple Simple	1961 1961	17 17	—		Mild Borderl.			+		Enuresis —	Under treat. Remission
6	1948	MM	Catat. Catat.	1966 1968	18 20	2	Severe			+			Sexual offence at 12 —	Chronic w. deter. Chronic w. deter.
7	1950	MM	No sympt. Hebephr.	1967	17			Mild			+		Frail constitution —	Defect
8	1950	MM	Simple Simple	1964 1967	14 17	3		Mild Borderl.			+		Premat., asphyxia, icterus	Part. remiss. Part. remiss.
9	1941	FF	Hebephr. Hebephr.	1968 1968	17 17	—	Severe			+			— —	Deter. Deter.
10	1952	FF	Simple Simple	1968 1968	16 16	—	Borderl.			+			— —	Unchanged Unchanged

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one. The twin method can add confusion and bewilderment if the psychological ground of material is not considered.

MZ twins, though with an identical genotype, develop their own personality struggling each one for his affirmation in the outer world as everybody else, and also in the secluded society of twinship, with arrangements and strategies that are different from those of the single born.

If a mental disease occurs at an age when personality has acquired individuality, the psychological reaction will relate itself to previous conditioned behavior, raising the problem of different diagnosis in cotwins.

Metabolic deficiency cannot be measured with a meter related to phenotypic mental symptoms: the distance from gene action to behavior, thinking, and affectivity is wide and indirect, so that the same genotypic want may raise different expressions within certain limits. Discordance in a pair of MZ twins is strictly in accordance with discordance in nosology. So, the diagnosis of the " healthy " cotwin in the samples studied by many authors is rarely that of an individual *free* from mental symptoms. Different expressivity in four of our pairs (4, 5, 7, 8) can be related to physical and psychological variables (infections, stress, parental attitude, etc.), but they are only concomitant events, never determinant.

Specificity is an oustanding feature of our sample: no cotwin showed symptoms that could be ascribed to another variety of the schizophrenic disease. No overlapping of symptoms was present.

The four cases with a severe form shared severity even when the disease had a dyschronic onset. Differences were present in mild forms.

Stability is not a property of the disease: cure, improvement, remissions, relapses, chronic defectual course, deterioration are characteristics which vary in each type. During the last 20 years treatment has modified the rhythm and course of the disease. In our sample we had defectual, unchanged, improved course, but in none we can offer a prognosis.

At the end of our study we can say that *ergon in schizophrenia obeys a genetic property.* If a disease is a polygenic one, a major gene acts — with its loss of activity — in a specific way. Severity is related to the want of the gene and to the coaction of the constellation of genes involved.

Instability can be explained with the metabolic attempt — successful or not — of regaining homeostasis.

Onset and dyschronia. The age at which our sample was examined does not allow general conclusions. Onset follows the rules of classical nosology. The paranoid case was the later in onset at age 23. Catatonic cases revealed themselves with acute excitement at ages 17 and 18 in the first born cotwin and after two years in the second born. Simple schizophrenia was detected slightly earlier than the hebephrenic one in two cases.

Schizophrenia is not always an acute disease: we can say that diagnosis is not really made but when the pot is filled and pours. Often psychotic personality is stud-

ied retrospectively, but it is impossible to establish a rule for the kind of behavior that will develop schizophrenia: every time we tried to foresee a diagnosis only on the ground of personality traits, we failed.

Anyway, the phenotypical expression occurs in each variety at almost a specific age. The largest portion of hebephrenic and simple type (94%) occurs at age 15-19; that of paranoid type, at age 25-35 (70%). Only 2% of schizophrenic cases develop before 14, and 6% after 45. That means that, in the course of life, still unknown biological rhythms occur, during which a hereditary failure may manifest itself. The degree of want of one or more interacting genes becomes evident in such new metabolic adjustments.

Whether different genes are involved in types of schizophrenia, or the wanting of a gene information gives different behavioral and conceptual symptoms at different ages, is a topic which deserves a long discussion that we shall not afford at this time.

In our sample we tried to study all possible variables that could explain dyschronia (cases 2, 4, 6, and 8) and discordance (case 7).

Birth order and weight. In three pairs (4, 6, and 8) the first born was the first to develop symptoms; in two pairs, the second born. No differences over 50 g in weight were present in three pairs (4, 6 and 8), one of which showed prematurity, asphyxia, low weight (1200-1220 g), and delayed development: the first born — IQ = 90, normal EEG and physically stronger — showed symptoms three years sooner than his cotwin — IQ = 80, dysrhythmic EEG, and protracted enuresis. In case 2, the heavier fell sick two years later, and in case 7, the one severely affected.

In one pair (4) the earlier schizophrenic twin suffered from severe enteritis, delayed physical development.

The passive cotwin showed symptoms earlier in two cases (4, 6), the dominant in two (2, 7); in case 8 dominance was alternate.

School records did not offer discordance, and intelligence tests were the same in each pair, except case 8.

Parental attitude was claimed in all cases as being the same for both twins.

The first to collapse in case 6 was the victim of a sexual offence at twelve.

As a conclusion, we can say that in our small series of schizophrenic MZ twins the temporal dimension of one or more genes was shortened, and that failure occurred during a change of biological rhythms.

In a disease as schizophrenia, phenotypic expression is only a phase of it, and dyschronia or discordance in a MZ pair cannot be accredited to a single physical or psychological variable, but to more concomitant factors.

Last but not least is the clinical belief that a hereditary disease is not present until phenotypical symptoms of *that* type are evident: schizophrenia is such a complex syndrome that we are still struggling for defining its limits, varieties, and symbols.

References

Bini L., Bazzi T. (1967). Trattato di Psichiatria. Ed. Vallardi, Milano.

Birch H. G., Hertzig M. E. (1967). Etiology of Schizophrenia. In J. Romano: Origins of Schizophrenia.

Böök J. A. (1960). A genetic and neuropsychiatric investigation of a North-Swedish population. Acta Genet. (Basel), **4**: 1-133.

Gedda L. (1951). Lo Studio dei Gemelli. Ed. Orizzonte Medico, Roma.

Gedda L., Braconi L. (1966). The twin method in the study of psychoses and psychoneuroses. Proc. 4th Mon. Cong. Psychiat., Madrid.

Gedda L., Brenci G. (1969). Biology of the gene: the ergon/chronon system. Acta Genet. Med. Gemellol., **18**: 329-379.

Gottesmann I. I., Shields J. (1966). Schizophrenia in twins. Br. J. Psychol., **112**: 809.

Gottesmann I. I., Shields J. (1967). A poligenic theory of schizophrenia. Proc. Nat. Acad. Sci. USA, **581**: 199.

Hanhart E. (1965). Die Genetischen Problem der Schizophrenien. Acta Genet. Med. Gemellol., **14**: 13-40.

Kallmann F. J. (1946). The genetic theory of schizophrenia. Am. J. Psychol., **103**: 309.

Kringlen E. (1967). Heredity and Social Factors in Schizophrenic Twins. In J. Romano: Origins of Schizophrenia.

Johanson E. (1958). A study of schizophrenia in the male. Acta Psychiatr. Scand. (Suppl. 125), 33.

Luxenburger H. (1934). Die Manifestationswahrscheinlichtkeit der Schizophrenie in Lichte der Zwillingsforschung. Z. Psych. Hyg., **7**: 174.

Mitsuda H. (1967). Clinical Genetics in Psychiatry. Osaka.

Pollin W., Stabenau J. R., Mosher L., Tupin J. (1966). Life history differences in identical twins discordant for schizophrenia. Am. J. Orthopsychiatry, **36**: 3.

Romano J. (1967). The Origins of Schizophrenia. Excerpta Medica Foundation, Amsterdam.

Rosenthal D. (1960). Confusion of identity and frequency of schizophrenia in twins. Acta Gener. Psych., **3**: 297.

Rosenthal D. (1967). An Hystorical and Methodological Review of Genetic Studies in Schizophrenia. In J. Romano: Origins of Schizophrenia.

Slater E. (1953). Psychotic and Neurotic Illnesses in Twins. Her Maj. Stat. Off., London.

Slater E. (1958). A monogenic theory of schizophrenia. Acta Genet. (Basel), **1**: 50.

Shultz B. (1956). Zur Frage der Erblichkeit der Schizophrenie. Acta Genet. (Basel), **5**: 51.

Tienari P. (1963). Psychiatric illnesses in identical twins. Acta Psychiatr. Scand. (Suppl. 171), 39.

Zazzo A. (1960). Les Jumeaux: le Couple et la Personne. Press Univ. France, Paris.

Riassunto

Sono state esaminate dieci coppie di gemelli MZ, di cui otto MM e due FF, con almeno un cogemello affetto da schizofrenia. La malattia è risultata concordante in quattro coppie, discordante in una e parzialmente concordante nelle altre cinque.

Il tempo d'insorgenza della malattia è risultato lo stesso in cinque coppie, mentre ha presentato una differenza di tre anni in due coppie e di uno-due anni in altre due. La concordanza nel tempo d'insorgenza non è apparsa in relazione alla gravità della forma.

Résumé

Dix couples de jumeaux MZ (huit MM et deux FF), avec au moins un membre atteint de schizophrénie, ont été examinés. La maladie s'est démontrée concordante chez quatre couples, discordante chez une, et partiellement concordante chez les autres cinq.

Le temps de début de la maladie a été le même chez cinq couples, mais a différé de trois ans chez deux couples et de un-deux ans chez deux autres. La concordance dans le temps de début n'est pas en rapport à la gravité de la forme.

ZUSAMMENFASSUNG

Es wurden zehn EZ-Paare (acht ♂ u. zwei ♀) untersucht, bei denen wenigstens ein Paarling an Schizophrenie litt. Das Leiden erwies sich bei acht Paaren konkordant, bei einem Paar diskordant und bei den übrigen fünf Paaren teilweise konkordant.

Bei fünf Paaren war die Krankheit gleichzeitig aufgetreten; bei zwei Paaren betrug der Unterschied drei Jahre und bei den anderen beiden Paaren ein bis zwei Jahre. Es zeigte sich kein Zusammenhang zwischen der Konkordanz der Auftrittszeit und der Schwere des Leidens.

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