PSYCHIATRIC AND CYTOGENETIC INVESTIGATION OF A FAMILY WITH "FAMILIAL" SCHIZOPHRENIA

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In the previous work by the same authors (12), data were submitted concerning relatively pronounced, but atypical deviations in the karyotype of schizophrenic patients, coming from families having one or more members affected with schizophrenia. Aiming more accurate determination of the role played by the genetic factor for the occurrence of "familial" schizophrenia, the authors assumed the task of carrying out detailed psychotic and cytogenetic investigation of patients with schizophrenia and healthy subjects of different generations — all members of the same family. Ten individuals are investigated from three generations of a family, in which the father I. Y. J. (F-2 V) is affected with schizophrenic disease since adolescence (running a course with attacks) and subsequently, three of his six descendants consecutively develop schizophrenia (his seventh child died from "varicella" on the first year of life). Metaphasic plates of lymphocytes from the peripheral blood, cultivated according to the method of Moorhead and assoc. as modified by M. Tzoneva-Maneva, were used for the cytogenetic analysis. The preparations were stained after the Romanovski-Gimsa method.

The psychiatric investigation provides evidence for multiple psychotic involvement of the father's progenitors (see genealogical tree — fig. 1): his grandfather (P I) exhibited characterologic abnormality ("unbalanced state"), whilst his father (F-1 III) several times in his life-span, in accordance with past history data, "became abnormal" with inadequate behaviour. Two of the father's cousins in the male line of descent (F-2 II and F-2 I) were affected with insanity (no more data available about them).

I. Y. J. 's mother was mentally healthy, but in her descent too, aberrations are detected of the psychotic health in two of her sister's sons (nephews).

The illness of I. Y. J. dates back to early abolescence; he is a full orfan and his social background is characterized by heavy living conditions. The schizophrenic disease in the latter case shows a course with numerous hallucinatory-paranoid attacks, followed by full remissions. His first sister V. Y. T. (F-2 III) sustains at the age of 35, a psychotic affection of depressive nature, occurring in connection with psychic trauma (probably reactive state). She had three children before falling ill (at present aged from 29 to 32 years) and none of them shows psychotic abnormalities. The second sister (F-2 IV) was affected with schizophrenia with hallucinatory-paranoid picture, running a course with repeated attacks and adequate remissions, at the age of 24, immediately post partum. She had four children and in none

of them a psychic disease is discovered (age ranging from 11 to 27 at the time of investigation).

Among the members of I. Y. J. 's offspring (aged between 20 and 35 years), merely two children — Y. I. J. (F-3 X) and P. I. J. (F-3 XIII) display psychopatic development of the personality, the former—of the type of affective disbalanced psychopathy with susceptibility towards cho-

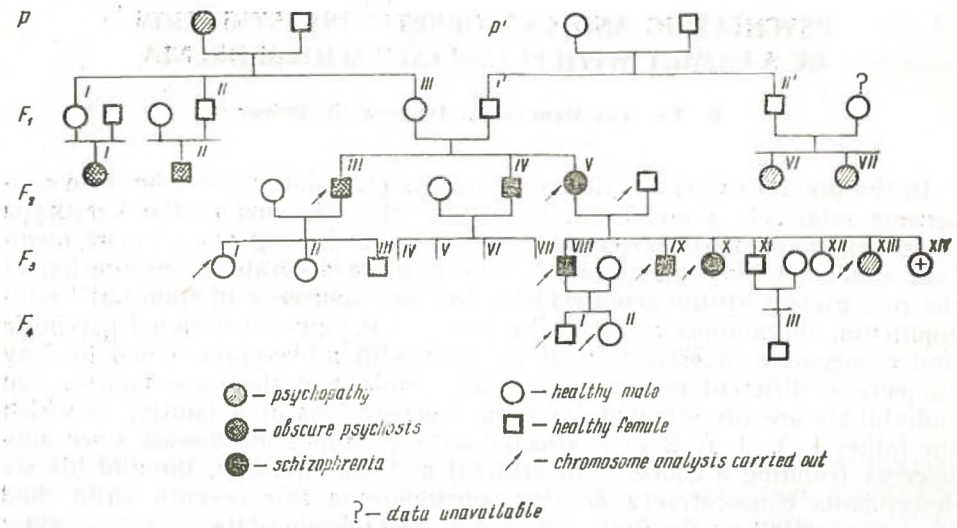

Fig. 1

leric explosions, and the latter — of the psychasthenia type. The first three children are affected with schizophrenia — VI. I. P., D. I. J. and Y. I. J. (F-3 VII, IX, X), all of them with hallucinatory-paranoid picture and running a course with repeated attacks and full remissions (merely in I. Y. J. remissions are concerned with partial restoration). The oldest sister fells ill at the age of 32, during lactation period following the second childbirth, the second one — at 20 years and the third — at 23 years with the interference of chronic alcoholic intoxication.

The offspring of the fourth generation (two from a schizophrenic mother and one — from a healthy mother) do not reveal psychopatic deviation (at the age ranging from 5 to 10 years).

It is of interest to point out that the only unaffected by the psychosis up to the moment of the present study, are the children who left very early their paternal home (and family) and resettled in far away places, thus escaping from the distressing familial environment and attitude of neighbours and friends in the village. The remainder (three children), apart of the hard childhood, vith frequent schizophrenic attacks on behalf of the father (during which he became also aggressive), live under conditions of being treated as children of an "abnormal father'' and later on, after the illness of the oldest daughter, also under the constant threat of "hereditary'' disease.

It is worth mentioning also the uniformity in the course and clinical picture of the schizophrenic disease in the different family members: — attacks with hallucinatory — paranoid nature, with full remissions even in instances of manifold repeated attacks (the only exception in this respect is Y. I. J.). A rather unfavourable course of schizophrenia in hereditary "burdening" is being reported in the pertinent literature (7, 9, 12, 45, 46), but many authors (22, 23) have not come across a similar dependence, some of them (1, 39, 44) emphasizing the more favourable course established among the relatives of patients with periodic schizophrenia. Literature data are contradictory insofar simila rity of the clinical picture in patients with "familial" schizophrenia is concerned. Coincidences and differences equally in the form and course of psychosis in the members of a family have been reported in varying percentage (1, 4, 5, 12, 21, 23, 44). Some authors (5) on the other hand, even derive the nosological unity of the various forms of schizophrenia on the basis of differences existing. Insofar the mode of explanation is concerned in analogous manifestation and course of the disease in different members of a single family, apart of the role played by genetic factors, the significance is also pointed out of the so-called psychodynamic factors — that is, the influence exerted by the familial milieu via psychogenic routes (23, 48, 49). The early onset of psychosis, related with the generation cycle (puerperium and lactation) in two of our patients is likewise of interest.

The results of the cytogenetic investigations in affected and healthy individuals of the family reviewed (see table 1) do not reveal the presence of any kind of typical chromosome aberration. Mostly pronounced karyotype changes are established in two of the studied patients with schizophrenia (F-3 IX and F-3 X), represented by numerical and structural changes in F-3 IX and high per cent numerical alterations in F-3 X. It should be remembered however, that the schizophrenic members of the family are concerned, studied during a psychotic attack in the course of active therapy with chlorpromazine (in the former also electro-shock). Next, according to degree of aberrations, rank F-2 III and F-2 V. In the former, aberrations are observed in the karyotype, both to the left and right (monosomes and trisomes), whilst in her brother — a high per cent of cells with monosomes. Leftside abberrations are likewise established in the wife of F-2 V, but in comparatively lesser degree. Aberrations in the fourth schizophrenic patient are negligible (F-3 VIII) — the oldest daughter of F-2 V — exhibiting merely isolated monosomes. In the remaining mentally healthy individuals, the single aberrations are within the limits of derangements in the karyotype of clinically healthy subjects, established by two of the authors of the present paper (17) and other authors as well (36).

The circumstance that mostly pronounced deviations are established in the two schizophrenic patients, studied during psychotic attack and treatment carried out with neuroleptic means, is in favour of the conception for the secondary nature of these alterations, which could eventually be connected with the psychosis present or preparation administered. The studies performed by one of the authors of the present paper on the effect, exerted by certain antibiotics of the tetracyclin group upon the mitotic activity and leukocytic karyotype of human peripheral blood, cultivated in vitro, demonstrate marked disorders in the cell division processes and in the struc-

Table 1

№	Name Sex	AGE	Diagnosis	Condition during investigation	Treatment	Kinship with I. Y. J.	Number of chromosomes							Karyotype
							45	45	46	47	47			
1	IYJ m	55	Schizophrenia	Remission A	—		10	2	45	—	—	57	7	44+XY, 43+XY = monos. E, 70+XY = monos. A, D, 6
2	VVT f	53	Reactive psychosis	Healthy	—	Sister	3	1	37	3	1	45	8	44+XY, 43+XX = monos. E, 44+XXX, 47+XX+1 no centr. fragment
3	IMJ f	54	Healthy	Healthy	—	Wife	3	5	62	—	1	71	6	44+XX, 44+XX with isochr. X dil. chr. 2, 44+XO, 43+XX-monos. C, not divided chrom. E, F
4	VIP f	32	Schizophrenia	Remission A	—	Daughter	1	1	37	—	—	39	4	44+XX
5	DIJ f	30	Schizophrenia	II attack	Chlorpromazine + electroshock	Daughter	—	—	26	2	—	28	4	44+XX, isochromosome X, dil. 1. trisomia 19
6	YIJ m	29	Psychopathy + schizophrenia	Exacerbation	Chlorpromazine	Son	15	14	70	—	1	100	11	44+XY, 43+XY-monos. E. 6 mon. E6, 39+XY- mon.C,D,E,F F, 40+XY, mon. A, 13, 15, E, 41+XY-mon. A,B,D
7	PIJ m	22	Psychopathy	Psychopathy	—	Son	—	1	43	1	—	45	9	44+XY, 45+XY-tris. E
8	NTS m	31	Healthy	Healthy	—	nephew	1	—	18	1	—	20	2	44+XY, 44+XXY
9	DDI f	10	Healthy	Healthy	—	Grandchild	3	2	12	—	—	17	3	44+XX, 44+XO, 39+XO-mon, 10, 11, 12 and 22
10	KDI m	5	Healthy	Healthy	—	Grandchild	—	2	4	—	—	6	1	44+XY

ture of chromosomes (19). After discussing the facts thus outlined, the assumptions of eventual cause — effect relationship existing between the stated substantial aberrations within the karyotype and the activity of viral agents or developing autoimmune processes in the course of schizophrenic disease are far from being inconsistent. It is well known that there exist data for the role played by vira (26, 33, 47) and by autoimmunization as well (27, 28, 29, 30, 31, 32) in the production of chromosome aberrations. There is evidence on the other hand, in favour of the hypothesis for etiopathogenetic relationship existing between schizophrenia and an infectious (viral) factor (3, 8, 10, 15, 16, 20, 35, 37, 40) as well as phenomena of autoimmunization (2, 6, 11, 13, 14).

The leftside aberrations, disclosed in the wife of F-2 V are of comparatively low percentage (12%) as compared to those in her husband (25%) and son (F-3 X — 29%). By rule, abnormalities of similar type could easily be attributed to technical causes (chromosome loss) and yet, in the case considered, it concerns a percentage exceeding the usually acceptable one. The latter deviation could be also related to the advanced age (55 years), which is equally valid for her husband and his sister.

The evidence herein reported as well as analogical investigations, made by other authors (24, 25 etc.) does not warrant drawing a conclusion concerning the relationship between schizophrenia and clear-cut chromosome aberrations. On the contrary, it is rather impressing that the aberrations observed are not the cause, but rather the consequence of a developing morbid process. Despite of that, the picture of the genealogical tree, exhibiting considerable psychotic (schizophrenic) morbidity, both in descending line and colaterally, is a prove for the eventual role played by genetic factors in the development of these psychoses. Such an assumption is in accordance with the conception of some authors (24, 38, 42) for the polygenic conditioning of the hereditary predisposition towards schizophrenia. It is illogical however, to ignore (in the present discussion) the role played by the general psychotraumatization of the affected family members, as well as of the eventual contagiosity (viral agent?).

With the goal to clarify the impression created by the studies hitherto carried out in this field, i. e. that the atypical aberrations in the karyotype are secondary (and not causative) phenomena, it is mandatory to further investigate the karyotype in the same patients — in the state of psychosis and out of it, in the course of definite therapy of psychosis and before its initiation as well.

Inferences

1) The schizophrenic disease in the five patients, members of the same family, runs a uniform course.

2) The chromosome aberrations in the patients investigated with "familial" schizophrenia appear to be aspecific.

3) The psychogenetic parallel in the family members studied does not reveal regular relationship between the psychotic disease and the karyotype: in most of the healthy and affected subjects, a normal karyotype is established in a larger number of the cells; numerical and structural aberrations are detected merely in isolated cells. Nevertheless, the most strongly pro-

nounced karyotype changes are established in two of the schizophrenic patients, investigated during the psychotic attack and neuroleptic treatment.

4) Chromosome aberrations in the schizophrenic patients studied, are, in all likelihood, secondary in nature.

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ПСИХИАТРИЧЕСКОЕ И ЦИТОГЕНЕТИЧЕСКОЕ ИЗУЧЕНИЕ СЕМЬИ С „СЕМЕЙНОЙ" ШИЗОФРЕНИЕЙ

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РЕЗЮМЕ

Исследованы клинически и цитогенетически больные и здоровые члены трех поколений одной семьи. Из данных цитогенетического изучения нельзя сделать вывод о связи шизофрении с определенными хромосомными отклонениями. Отклонения в кариотипе — численные и структурные, устанавливаются у лиц в остром психозе и периоде интенсивного лечения. Эти отклонения расцениваются как вторичные (связанные с используемыми медикаментами, как и в результате случайных инфекционных агентов или развивающихся аутоимунных процессов).

Картина родословного дерева со значительной психической (шизофренической) заболеваемостью, как по нисходящей, так и по боковой линиям, указывает на возможную роль генетических факторов (полигенная обусловленность наследственного предрасположения к шизофрении).