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Essential Isochronic Epilepsy in MZ Twin Pairs

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SUMMARY

A total of 45 twin pairs (19 MZ and 26 DZ), with one or both members affected by essential Generalized Epileptic Attacks, have been drawn out of the Mendel Institute's twin file. Concordance was observed in 18 : 19 MZ, but only in 3 : 26 DZ twin pairs.

Analysis of the 18 MZ concordant twin pairs has shown (1) concordance of clinical form in 17 pairs, (2) concordance in the age of onset in 15 pairs, and (3) concordance of expression (frequency of generalized attacks) in 13 pairs.

By epilepsy we mean a tendency to manifest a particular pattern of the central nervous system which may be provoked in any subject provided there is a lowering of the so-called convulsive threshold.

Essential epilepsy, according to the centroencephalic concept of Penfield and the Marseille School, refers to the clinical manifestation of a paroxysmal disorder in the electrogenetic regulation by the reticular formation. These bioelectric disorders are epiphenomena of biochemical changes.

In the WHO classification, essential epilepsy was indicated as Generalized Epileptic Attacks. This title includes the centroencephalic forms of epilepsy (grand mal, petit mal, myoclonic petit mal) and other attacks (hyperpyretic convulsions, pavor nocturnus, and somnambulism) which, according to many physiopathologists, should not be classified as epileptic. In our opinion, they should be considered as microforms of essential epilepsy.

In classifying the various forms, the idiopathic or essential character is given to those cases with no anamnestic or clinical reference to those factors usually found in focal epilepsy (prenatal or congenital; delivery trauma; toxic, infectious, degenerative or vascular postnatal encephalopathy; cranial trauma; fulguration), beside that of a genotypic disposition.

The genetic studies on epilepsy, at first simply based on empiric observations of the frequency of the condition in different families, were later improved through a modern statistical approach (Lennox et al, 1940), while Kimball and Hersch (1955), with the use of electroencephalographic techniques, revealed the high incidence (approximately, 60%) of a dysrhythmia in the lineal ascendents and collateral members.

Tab. I

No.	File no.	Sex	Clinical form	EEG	Onset (in months)		Frequency of attacks	Famil. of epilepsy
					Age	Differ.		
1	994	FF	Grand mal Grand mal	+ spec. + spec.	24 24	0	disc.	+
2	1855	FF	Petit mal Petit mal	+ spec. + spec.	60 60	0	conc.	—
3	1150	MM	Pavor nocturnus Pavor nocturnus	+ aspec. + aspec.	101 108	7	conc.	—
4	5136	FF	Pavor nocturnus Pavor nocturnus	— —	24 24	0	conc.	—
5	5537	FF	Petit mal Petit mal	— —	156 144	12	conc.	+
6	139	FF	Petit mal —	+ spec. neg.	17 —	—	—	—
7	647	FF	Grand mal Grand mal	neg. neg.	24 24	0	disc.	—
8	5334	FF	Grand mal Grand mal	+ spec. + spec.	20 10	10	conc.	+
9	1667	MM	Grand & petit mal Grand mal	+ spec. + spec.	3 10	7	disc.	+
10	6398	MM	Grand & petit mal Grand & petit mal	neg. neg.	4 4	0	conc.	—
11	6439	FF	Grand mal Grand mal	+ spec. + spec.	52 56	4	conc.	—
12	676	FF	Petit mal Petit mal	+ aspec. + aspec.	72 72	0	conc.	+
13	6501	MM	Pavor nocturnus Grand mal	neg. + aspec.	72 1	71	disc.	—
14	10596	MM	Hyperp. crises Hyperp. crises	— —	72 72	0	conc.	+
15	9312	MM	Petit mal Petit mal	+ spec. + spec.	53 53	0	disc.	—
16	10387	MM	Grand mal Grand mal	+ aspec. + aspec.	18 18	0	conc.	—
17	539	MM	Grand & myoclonic petit mal Grand & myoclonic petit mal	— —	8 12	4	disc.	—
18	12200	MM	Grand mal Grand mal	+ aspec. + aspec.	8 8	0	conc.	+
19	5141	FF	Pavor nocturnus Pavor nocturnus	— —	28 28	0	conc.	+

NOTE. EEG, + spec. = centroencephalic type (infracritical or critical); + aspec. = infracritical dysrhythmia (in one or more tracings); neg. = normal.

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The investigations carried out with the twin method by Stroessler, Sanders, Rosanoff, Schulte, Conrad, Lennox, Alström, Gedda, Slater, Braconi, Vogel, and others have contributed in establishing the proportions between the causal factors of the disease. Rosanoff et al (1931), Conrad (1940), Lennox (1951), and Braconi (1962) have demonstrated a specific hereditary factor in the genesis of epilepsy, either symptomatic or idiopathic, in about 65% of the cases studied.

As far as essential epilepsy is concerned, the various authors found a very high concordance in the manifestation of the condition in MZ twins (Lennox 84%, Conrad 96%, Braconi 91%), whereas in DZ twins the concordance was considerably lower (Conrad 4.3%, Braconi 50%). In our preliminary studies we found that the concordance of essential epilepsy in DZ twins was of 15.38% (4 out of 26 pairs). (See Tab. II).

Tab. II

		Concordance		Discordance		Total
		N	%	N	%	N
DZ	Idiopathic epilepsy	4	15.38	22	84.62	26
MZ	Idiopathic epilepsy	18	94.45	1	5.55	19
	clinical form	17	94.12	1	5.88	18
	age of onset	15	83.33	3	16.67	18
	frequency of attacks	12	66.66	6	33.34	18

The aim of our research was to study the idiopathic Generalized Epileptic Attacks in MZ twin pairs in relationship to the phenogenetic intrapair concordance regarding the clinical form, age of onset, and frequency of attacks.

The pairs studied were taken from the Twin Register of the Mendel Institute, Rome. To determine the age of onset, the first episode of fits was considered, and the final diagnosis was based on the development of the form (see the case of hyperpyretic convulsions followed by attacks of great pain). The difference in the age of onset of attacks for each twin was significant if over four months in the case of twins up to three years old and if over twelve months for twins over four years old. As far as the frequency of the attacks is concerned, the findings were considered as concording in those twin pairs which had a difference of no more than 20% in the number of attacks.

The investigations, briefly set out in Tab. I, gave the results reported in Tab. II.

In the MZ twin pairs (9 MM and 10 FF) with idiopathic epilepsy we found 94.45% concordance (18 pairs out of 19). In the 18 pairs with concording epilepsy we found 94.12% concordance for the clinical form, 83.33% for the age of onset, and 66.66% for the frequency of attacks.

These investigations lend further support to previous studies using the twin test showing that essential epilepsy is of a hereditary nature. Furthermore the high concordance of the age of onset shows that also this aspect of the disease is of a hereditary nature, and that the morbid genotype of the epilepsy has its own *chronon* (Gedda and Brenci, 1969), and the time parameter belongs to the hereditary patrimony.

References

Braconi M. (1962). La ricerca gemellologica nell'epilessia. Acta Genet. Med. Gemellol., **11**: 138-157.
Braconi L. (1963). L'epilessia come espressione di un tratto ereditario. Proc. 2nd Int. Congr. Hum. Genet., Roma.
Conrad C. (1940). Die erbliche Fallsucht. Handbuch der Erbkrank. Thieme Verlag, Leipzig.
Gedda L. (1951). Lo Studio dei Gemelli. Ed. Orizzonte Medico, Roma.
Gedda L., Brenci G. (1969). Biology of the gene: the ergon/chronon system. Acta Genet. Med. Gemellol., **18**: 329-379.
Kimball O. P., Hersh A. H. (1955). The genetics of epilepsy. Acta Genet. Med. Gemellol., **4**: 131.
Lennox W. G., Gibbs E. L., Gibbs F. A. (1940). Inheritance of cerebral dysrythmia and epilepsy. Arch. Neurol. Psychiatr., **44**: 1155.
Rosanoff J., Handy L. M., Rosanoff I. A. (1931). Etiology of epilepsy. Arch. Neurol. Psychiat., **31**: 1165.
Vogel F. (1965). Genetic aspects of the EEG. EEG Clin. Neurophysiol., **19**: 196.

Riassunto

Dalla cartoteca dell'Istituto Mendel sono state ricavate 45 coppie di gemelli, 19 MZ e 26 DZ, con uno o ambedue i cogemelli affetti da Attacchi Epilettici Generalizzati essenziali. È stata riscontrata concordanza in 18 : 19 coppie MZ e solo in 3 : 26 coppie DZ.

L'analisi delle 18 coppie MZ concordanti ha rilevato inoltre: (1) concordanza di forma clinica in 17 coppie, (2) concordanza dell'età di insorgenza in 15 coppie e (3) concordanza di espressione (frequenza di attacchi generalizzati) in 13 coppie.

Résumé

Un échantillon de 45 couples de jumeaux (19 MZ et 26 DZ), dont l'un ou les deux membres atteints de Attaques Epileptiques Généralisées essentielles, a été tiré du régistre géméllaire de l'Institut Mendel. La maladie était concordante chez 18 : 19 couples MZ et seulement chez 3 : 26 couples DZ.

L'analyse des 18 couples MZ concordants a aussi démontré: (1) concordance de forme clinique chez 17 couples, (2) concordance de l'âge de début chez 15 couples et (3) concordance d'expression (fréquences des attaques généralisées) chez 13 couples.

Zusammenfassung

Aus der Kartothek des Mendel-Institutes wurden 45 Zwillingspaare gewählt (19 EZ und 26 ZZ), von denen einer oder beide an allgemeinen essentiellen epileptischen Anfällen litten. Bei den EZ betrug die Konkordanz 18:19 bei den ZZ-Paaren nur 3:26.

Eine Analyse der 18 konkordanten EZ-Paare ergab ausserdem: (1) bei 17 Paaren eine Konkordanz der klinischen Form, (2) bei 15 Paaren Konkordanz des Auftrittsalters und (3) bei 13 Paaren Konkordanz der Ausdrucksform (Frequenz der allgemeinen Anfälle).

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