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Cardiological Findings in Twins, with Special Reference to their Zygosity and Peristasis

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Introduction

The genetic importance of the cardiological status extends beyond the field of pathology to a number of signs within the physiological range. Twin studies have shown genetic influence on such parameters as the blood pressure (Mathers *et al.*, 1961), the X-ray appearance and ECG. Most of the older ECG studies (Parade, 1935; Kahler *et al.*, 1939; Joly *et al.*, 1949; Kabakov *et al.*, 1934; Blumberger, 1940) have, however, the drawback of purely qualitative estimation based, as a rule, on standard limb leads. More recent studies have indicated genetic variability in blood pressure, but these measurements were predominantly characterized by sex influences (Mathers *et al.*, 1961). This study aims at an analysis of the genetic implications of clinical and ECG findings in twins.

Methods

37 pairs of dizygotic (DZ) and 12 pairs of monozygotic (MZ) cardiologically sound twins of both sexes, age 10-15 (including 1 pair of 16 years) were examined first clinically, i. e. by palpation, percussion, and auscultation. A 12-lead ECG curve was then recorded in supine position and simultaneously, all under basic conditions.

Tab. 1. Age distribution in the sample

Years	10	11	12	13	14	15	16
MZ pairs	1	0	1	5	2	2	0
DZ pairs	4	2	4	7	10	10	1

The examining physician was not aware of the zygosity of the twins his examination being concluded before the results of the haematologic, dermoglyphic, and other analyses were known. The clinical attention was concentrated on a comparison of the quality of the heart sound or possible murmurs and other phenomena within each pair. That is why the findings were classified merely as concordant or discordant.

The ECG curves were classified as a first step on a qualitative basis as very similar, similar, and dissimilar. Features such as overall impression, heart rate, polarity of the waves and their general pattern have been included in this evaluation. Secondly,

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the PQ, QRS and QT_c intervals as well as the height (in millimeters) of Q, R, S, T have been analyzed by the method of paired analysis, as described by Osborne and De George (Mathers *et al.*, 1961), which expresses the average of the differences between the two members of the pairs of twins as mean intrapair variance v_1:

$$v_1 = \frac{\sum_{i=1}^{n} \cdot d_i^2}{2n}, \text{ where}$$

$d_i = x_i - y_i$ (the difference of data in the i-th pair) and n = number of pairs.

The F distribution is used to obtain the probability level of mean intrapair variances. In order to be able to compare the mean of the differences of any two data within a pair of twins with the mean of differences observed between two individuals in the study population with no relationship whatsoever, mean interpair variances v_2 have been calculated:

$$v_2 = \frac{\sum_{i=1}^{n} \cdot d_i^2 - \frac{(\sum a_i)^2}{2n}}{n-1}, \text{ where}$$

$a_i = \frac{x_i + y_i}{2}$ (the mean of the values of the i-th pair).

A comparison with v_1 is possible after multiplying this variance by 2. Again, the F distribution is used to test the significance of the $v_2 : v_1$ ratio in both MZ and DZ twins as well as the $v_1MZ : v_2DZ$ ratio. Results and discussion:

The clinical picture in MZ twins has been rated 10x similar, once dissimilar, one pair of twins escaped the clinical examination. In DZ twins it has been 18x similar, and 19x dissimilar.

The qualitative evaluation of the ECG curves classified them as very similar, similar, and dissimilar (cfr. Tab. 2). This kind of evaluation was considered justi-

Tab. 2

ECG	MZ	DZ
Very similar	8	3
Similar	4	23
Dissimilar	—	11

fied as a complement to the quantitation of the ECG data. No dissimilar curves have been observed in MZ twins: 8 times the curve has been considered very similar and four times similar. In DZ twins the ECG curve has been three times very similar, 23 times similar, and 11 times dissimilar. The probability of the distribution of very similar and similar findings not being dependant from the twins zygosity equals $P = 0.001$. Hence it may be stated on a 0.1% significance level that the distribution of very similar and similar findings depends on zygosity.

Thereafter, the differences of corresponsing waves within each pair have been calculated, and a mean difference d obtained.

The coincidence of $d \leq 1.5$, very similar ECG and similar clinical finding permits conclusions as to the twins' zygosity: if all three criteria are fulfilled, the twins' monozygosity is established on a $P = 0.95$ level. 8 out of 11 MZ twins fulfil this condition, as against one DZ pair out of 37. On the other hand, no conclusion as to the twins' zygosity is possible if these three criteria fail to agree.

The method of paired analysis estimates intra- and interpair differences of MZ and DZ twins. Each pair of MZ twins is not only genetically identical, but also of the same age and in the same socioeconomic status. In this the DZ twins are similar, but genetically they are different and on the same level as any siblings. Interpair differences, on the other hand, express the mean of differences between individuals that have nothing in common either in the genetic or peristatic respect, and whose ages differ; this must be borne in mind when estimating various ECG parameters. The age-group concerned in this study is 10-15 years (including one pair of 16 year-old MZ twins) who fall within the group of older school children in the usual classification by Ziegler, Mazo (1961) a. o. As was to be expected, all ECG values fell within the normal range. Resultant v_1 and v_2 variance ratio in MZ and DZ twins has been compared with the critical values of Snedecor's F_α (f_1, f_2) with $\alpha = 5\%$.

The mean intrapair DZ variance of $Tv_{1\text{-}6}$ obtained significantly greater than in MZ twins (v_1DZ : v_2MZ). For the same wave the MZ $v_2 : v_1$ ratio is statistically significant, i. e. the mean intrapair variance is significantly smaller than the interpair one. For the MZ R wave the $v_2 : v_1$ ratio is statistically significant in all unipolar precordial leads except V_3 the value of which lies hard on the limit of significance (cfr. Tab. 3). The results are not so clear-cut for the Q and S waves and consequently

Tab. 3

R-wave

	I	2	3	V1	V2	V3	V4	V5	V6
$MZv_2 : MZv_1$	4,205*	1,672	11,682*	6,782*	12,420*	2,654	4,565*	9,538*	11,044*
$DZv_1 : MZv_1$	1,813	2,342	2,432	1,333	2,948*	1,274	2,037	2,969*	3,410*
$DZv_2 : DZv_1$	2,444*	2,277*	1,859	1,112	1,566	2,696*	2,220*	2,086*	1,212

T-wave

	I	2	3	V1	V2	V3	V4	V5	V6
$MZv_2 : MZv_1$	2,084	3,826*	1,694	14,800*	3,817*	3,506*	7,203*	4,178*	15,245*
$DZv_1 : MZv_1$	1,270	1,728	1,313	7,960*	2,866*	2,664*	8,014*	6,189*	9,982*
$DZv_2 : DZv_1$	1,672	1,731	1,070	2,060*	3,101*	1,713	1,306	1,607	1,793

* = significant

have no bearing on our problem. Thus, the difference between MZ and DZ twins is best characterized by the Tv_{1-6} wave, and to a certain degree by the Rv_{1-6} (cfr. Fig. 1).

We used this study to refer our results to those of Mathers *et al.* (1961) who found considerable and significant intrapair: interpair ratios in MZ twins for the duration

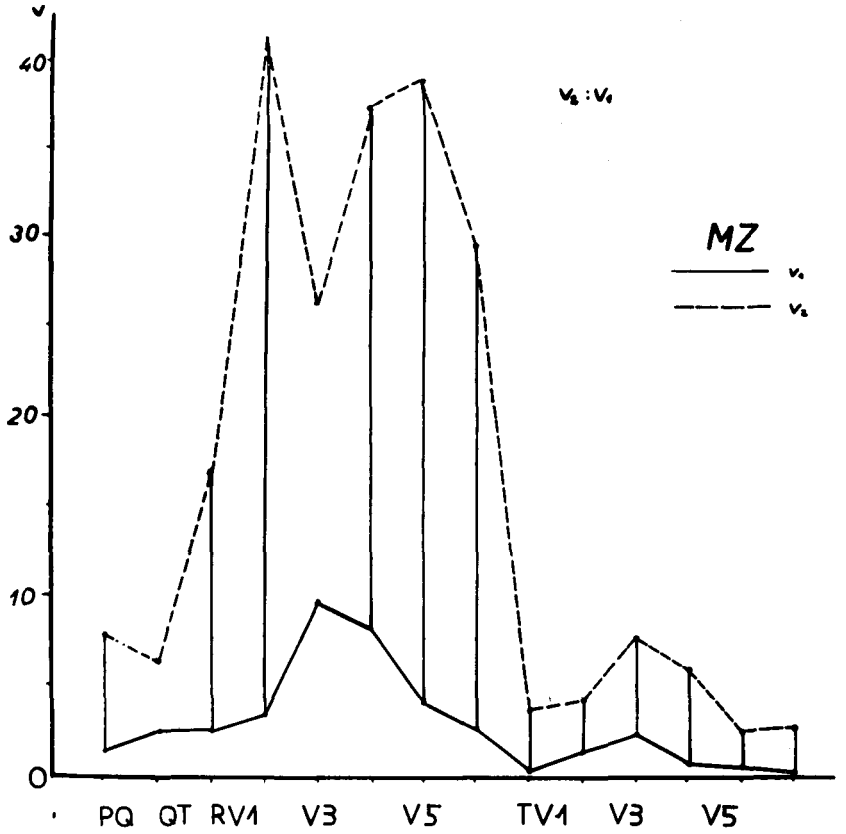

Fig. 1. The vertical ordinate indicates the $V_2 : V_1$ ratio in MZ. The horizontal ordinate shows the parameters tested. Vertical lines connecting the V_1 and V_2 values indicate significance of the ratio

of QRS and QT, and in the female intrapair MZ : DZ variance ratio. Both groups are, however, somewhat different, Mathers *et al.* dealing with grown-ups who were subdivided according to sex. Our results are presented on Tab. 4, the comparison with the above mentioned data is made on Tab. 5. The MZ variance ratio $v_2 : v_1$ has been found statistically significant only for the PQ interval, but not for QT_c or QRS. In spite of this difference it should be pointed out that our MZ $v_2 : v_1$ ratio

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Tab. 4. Mean interpair and intrapair MZ and DZ variance for PQ, QT, QRS

Zygosity	Comparison	n	Variance	F ratio
			P Q	
MZ	interpair	11	7,908	
	inter : intra			5,581**
MZ	intrapair	12	1,417	
	DZ : MZ			2,470*
DZ	intrapair	37	3,500	
	inter : intra			1,950
DZ	interpair	36	6,824	
			Q T	
MZ	interpair	11	6,408	
	inter : intra			2,607
MZ	intrapair	12	2,458	
	DZ : MZ			3,881*
DZ	intrapair	37	9,540	
	inter : intra			1,073
DZ	interpair	36	10,236	
			Q R S	
MZ	interpair	11	1,374	
	inter : intra			1,570
MZ	intrapair	12	0,875	
	DZ : MZ			0,803
DZ	intrapair	37	0,703	
	inter : intra			3,001*
DZ	interpair	36	2,110	

Tab. 5. Comparison of our results (left) with those of Mathers (right) for PQ, QT, QRS

			♂	♀
$MZv_2 : MZv_1$	PQ	*	*	*
	QT	(*)	*	*
	QRS	—	*	*
$DZv_1 : MZv_1$	PQ	*	—	—
	QT	*	—	*
	QRS	—	—	*
$DZv_2 : DZv_1$	PQ	—	—	—
	QT	—	—	—
	QRS	*	*	—

* = significant
(*) = just below the significance level
** = very significant

for the QT_c interval (marked by an asterisk in Tab. 5) is hard beneath the significance level. The PQ and QT_c variance ratio $v_1DZ : v_1MZ$ is statistically significant in the present study group, in Mathers only for the female QT and QRS. In our subjects the $v_2 : v_1$ DZ variance ratio is statistically significant for the duration of QRS, in Mathers for the male PQ and QRS (cfr. Tab. 4). We conclude that there is reasonable agreement between Mathers' and our results for PQ, QT_c and QRS in spite of the fact that both groups are rather disparate. Some border-line results suggest that the agreement would have been closer, had both groups been more numerous.

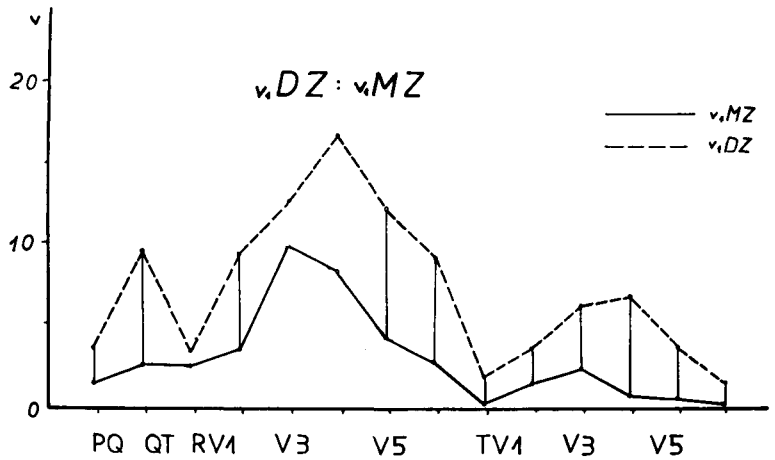

Fig. 2. The vertical ordinate indicates the v_1 MZ : v_1 DZ ratio. The horizontal ordinate shows the parameters tested. Vertical lines connecting the v_1 MZ and v_1 DZ values indicate significance of the ratio

This applies to the MZ PQ and QT_c intrapair: interpair ratios of variance, and more especially for the QT_c MZ : DZ variance ratio. This ratio is significant in our group even for the PQ interval (cfr. Figs. 1 and 2). These findings, too, suggest a strong genetic component of the variability of PQ and QT_c.

In spite of the great similarity of ECG findings in MZ twins more or less distinct differences remain within each pair. After deducting such factors as minor inexactitude in the placement of electrodes, possible peristatic influence must be considered. Setting the mean of R, S, T values in the unipolar chest leads as 100, a comparison of these data can be made within the MZ and DZ pairs on a percentile level. The percentage has been calculated for each pair separately and their means were obtained from all 12 MZ pairs and an equally numerous random selection of DZ twins. The Q wave has been omitted on purpose since its smallness would have unduly distorted the fault of measurement. The results show that (i) as could be expected, the differences are greater in DZ than in MZ twins, and (ii) the differences between the siblings expressed as percent of the mean R, S, T respective group values increase

both in MZ and DZ pairs, starting with the R wave and ending with the T wave. In other words, the above-mentioned differences tend to increase during a single heart cycle (cfr. Fig. 3).

The depolarizing and repolarizing dipoles run across the muscle cell in the same direction and cause electric stimulation of equal duration in every spot of its cross-section. Electromotor differences between genetically identical individuals can there-

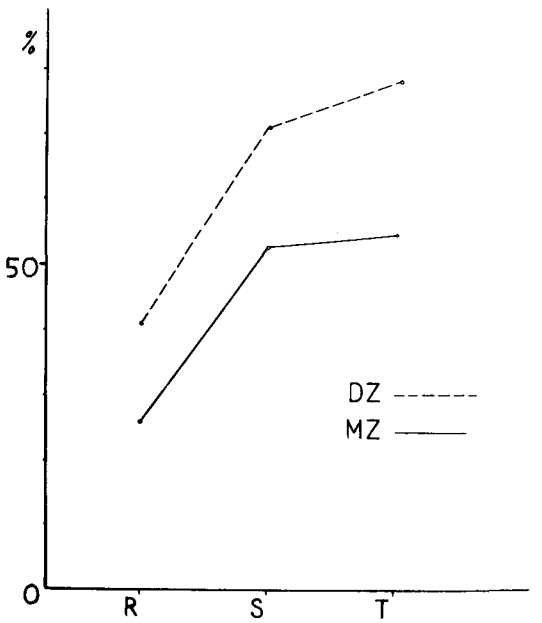

Fig. 3. Mean intrapair differences of individual waves in 12 MZ and 12 DZ pairs are expressed as ta percentage of the mean of the sum of the respective waves in 6 unipolar chest leads for each pair

fore be explained in terms of actual differences in the concentration of potassium, kreatin, glycogen a. o. ional carriers on the cell membrane together with other possible influences such as that of the tissue temperature. As the whole muscle-mass of the ventricles participates in the shaping of the QRS-T complex, it is conceivable that the growing differences of the consecutive phases of the ventricular complex are determined by a gradual increase of non-genetic influences. Should this observation prove to be constantly reproducible, the obvious explanation seems to lie in the actual biochemical status of the myocardium.

A comparison with the DZ group shows that the increase of the percentage differences in R-S-T waves runs almost parallel with values obtained in MZ twins but for the differences being greater. This leads to the conclusion that there is no apparent difference in the basic pattern of this increase in MZ as well as in DZ pairs.

Summary

37 DZ and 12 MZ twin pairs underwent a clinical and ECG heart examination. As to their zygosity, it is suggested that a concurrent similar clinical finding, very similar ECG and a mean intrapair difference of corresponding unipolar chest lead waves $d \leq 1.5$ definitely support monozygosity.

Paired analysis of the ECG curves shows that the difference between MZ and DZ twins is best characterized by Tv_{1-6} and, to a certain extent, by Rv_{1-6}. The same applies — in partial agreement with Mathers *et al.* — for PQ and QT_c intervals.

Considering the intrapair differences in both MZ and DZ twins, it was found that they tend to increase in the course of one cardiac cycle, thus indicating a gradual prevalence of peristatic factors.

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RIASSUNTO

37 coppie di gemelli DZ e 12 di MZ sono state sottoposte ad esame clinico ed elettrocardiografico. Per quel che riguarda lo zigotismo, uno stesso reperto clinico concordante, un elettrocardiogramma molto simile, e una differenza media intracoppia di onde corrispondenti alle derivazioni precordiali unipolari $d \leq 1,5$ sono decisamente in favore del monozigotismo. Una analisi comparata dei tracciati ECG dimostra che la differenza tra gemelli MZ e DZ è caratterizzata dall'onda Tv_{1-6} e, fino ad un certo punto, da Rv_{1-6}. Lo stesso vale per gli intervalli di PQ e QTc — in parziale accordo con la teoria di Mathers *et al.* Considerando le differenze intracoppia, nei gemelli sia MZ che DZ, si è trovato che esse tendono ad aumentare nel corso di un ciclo cardiaco, indicando una graduale prevalenza di fattori peristatici.

RÉSUMÉ

37 couples de jumeaux DZ et 12 de MZ ont été l'objet d'un examen clinique et électrocardiographique. Un tableau clinique pareil, un tracé ECG très proche, et une différence intra-couple moyenne des ondes correspondantes aux dérivations précordiales unipolaires $d \leq 1,5$ supportent, en définitive, un monozygotisme présomptif. Une analyse comparée des tracés ECG démontre que c'est l'onde Tv_{1-6} et, jusqu'à un certain degré, celle Rv_{1-6}, qui caractérisent le mieux la différence entre les jumeaux MZ et DZ. La même conclusion tient pour les intrevalles PQ et QTc, en accord partiel avec Mathers *et al.* Les différences intra-couple entre jumeaux MZ et DZ ont une tendence à augmenter au cours d'un cycle cardiaque, ce qui indique une prévalence graduelle des facteurs péristatiques.

ZUSAMMENFASSUNG

37 ZZ und 12 EZ Paare wurden einer klinischen und elektrokardiographischen Herzuntersuchung unterzogen. Hinsichtlich der Eiigkeit ergab sich daraus, dass der gleiche klinische Befund, ein ganz ähnliches EKG und eine durchschnittliche Differenz von 1,5 d korresspondierender Wellen innerhalb eines jeden Paares endgültig die Eiigkeit bestimmen.

Eine Vergleichsanalyse der EKG-Kurven zeigt, dass Tv_{1-6} und in einem gewissen Niveau auch Rv_{1-6} den Unterschied zwischen EZ und ZZ am besten kennzeichnen. Das Gleiche zeigt sich für die Überleitungszeit PQ und die Dauer von QTc — zum Teil nach der Theorie von Mathers *et al.* Bei Betrachtung der Unterschiede zwischen den Paarlingen bei EZ und ZZ stellte man fest, dass diese im Laufe des Herzzyklus zum Anstieg neigen, was für ein allmähliches Vorherrschen der peristatischen Faktoren spricht.