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Electroencephalographic Findings in MZ Twin Pairs, Discordant for Closed Head Injury

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Introduction

There has been much discussion whether symptoms, including EEG abnormalities, persisting a long time after a head injury are always of organic origin. The differences of opinion expressed in the literature probably arise from the difficulty in finding controls that are sufficiently comparable to the injured persons. An attempt was made to throw light on this question by studying MZ twins with head injuries, using their co-twins as controls.

This report is based partly on the monograph " A follow-up study of 128 closed head injuries in twins using co-twins as controls " (Dencker, 1958) and partly on a re-examination of the EEG records, which were included in that study.

Material and Methods

The material consists of 28 pairs of MZ twins. The series and relevant findings have been described in detail (Dencker, 1958, 1963).

The twins were compared for likeness in the following features: colour and structure of iris, colour and structure of hair, presence or absence of freckles, total number of ridges in the pulps of the fingers (5 classes), occurrence of whorls in the fingerprints, shape of the helix, tragus, incisura intertragica, tuberculum posterius auris, tips of ears, bridge of nose, nostrils from below and shape and size of lips.

Whenever there was the slightest doubt about the diagnosis, the blood groups were classified according to the ABO, MNS, Lewis and Rhesus (with the aid of the antiserums C, D, E, and c) systems and in one case also according to the P, Duffy and Kell blood systems and the Hp and Gm serum group systems. The gene frequencies for the blood groups were taken from a study of a Danish population (Gürtler, 1953) which should resemble the people of southern Sweden in anthropologic respects.

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If the frequency of a given degree of differences in more independent criteria in MZ pairs is A_1, A_2, A_3 etc. and in DZ pairs B_1, B_2, B_3 etc., then the proportion of MZ twins among all pairs of twins with this specific combination of differences will be:

$$W = \frac{A_1.A_2.A_3...}{A_1.A_2.A_3... + B_1.B_2.B_3...} = \frac{1}{1 + (B_1/A_1)\ (B_2/A_2)\ (B_3/A_3)...}$$

If the ratio between DZ and MZ pairs in the original material is q the formula will be $W = 1/[1+q\ (B_1/A_1)\ (B_2/A_2)\ (B_3/A_3)...]$ which can be used in the calculation for every single pair. W thus expresses the probability of monozygosity calculated on the basis of the observed intra-pair differences in a number of traits (Essen Möller, 1941; cf also Dencker et al 1961). Using this formula and the traits discussed the probability of being MZ was 98% or higher in this series.

Nineteen of the twin pairs were male and nine female. The age varied at follow-up from 10 to 55 years. The injured twins were re-examined 3 to 25 years after their accidents and their co-twins were used as control subjects.

Assessment of severity of head injury

The severity of the head injury was graded according to the length of the total post-traumatic amnesia, mainly in agreement with the scheme described by Denny-Brown (1945):

1st grade no amnesia
2nd grade amnesia lasting less than 10 minutes
3rd grade amnesia lasting less than 1 hour
4th grade amnesia lasting 1 to 24 hours
5th grade amnesia lasting 1 to 7 days
6th grade amnesia lasting more than 1 week

The probands and their co-twins were given a general, psychiatric and neurological examination, including a psychometric study.

Electroencephalographic examination

The EEGs were recorded with a 6-channel Kaiser machine from twelve electrodes, distributed in frontal, parietal, occipital and temporal regions. The hyperventilation test was done routinely. Already in the primary examination of the EEG records (E. Nyman) a high rate of electroencephalographic concordance was found between injured twins and their partners. These results are of great importance, especially for clinical neurologists, but electroencephalographists require more details of the records. Therefore these records were re-examined to get more detailed and systematically processed information about the corresponding findings.

The present re-examination was performed according to an EEG code, designed by one of the Authors (Sulg), for statistical data processing, adapted to the actual study. The EEG records were classified according to conventional principles as:

1. Normal
2. Borderline
3. Slightly abnormal
4. Moderately abnormal
5. Severely abnormal

In addition to the EEG code a scoring system including a *point scale* has been worked out to enable more detailed registration and comparison of the intra-pair differences (Tab. I). Discordant aberrations and abnormalities were weighted in points according to their degree of severity. For example, if there was a difference in alpha frequency of 1 c/sec between members of a pair, the two points were given

Tab. I. The point scale for the scoring of intra-pair differences *

Intra-pair difference	Points
DOMINANT ACTIVITY	
An intra-pair difference in alpha frequency; per 1 c/sec	2
A more pronounced instability, irregularity or asymmetry of alpha rhythm	1-2
A difference in mean voltage of more than 20 μV	1
An aberrant distribution of alpha rhythm	1
Poor or asymmetrical alpha blocking by eye opening	1
ABNORMAL ACTIVITY	
A discordant abnormality	2
A more pronounced abnormality of the same quality	1
The voltage more than twice the alpha amplit.	1
ACTIVATION	
Abnormality not present in resting record	2
Accentuating of abnormality seen during rest	1
CLASSIFICATION	
An intra-pair difference in the degree of abnormality ** according to the EEG code; for each step	1

* Discordant aberrations and abnormalities were weighted in points according to their degree of severity. For example, if there was a difference in alpha frequency of 1 c/sec between members of a pair, the two points were given to the twin with the lower frequency. These points, which always had a certain negative value, were counted separately for the proband and the partner. The total intra-pair difference was thus characterized by the sum of points that both twins scored.

** The five degrees of abnormality are mentioned above.

https://doi.org/10.1017/S1120962300012804 Published online by Cambridge University Press

to the twin with the lower frequency. These points, which always had a certain negative value, were counted separately for the proband and the partner. The total intra-pair difference was thus characterized by the sum of points that both twins scored.

Results

Generally we found a high rate of concordance between injured twins and their partners, whether the EEG patterns were normal or abnormal (Figs. 1 and 2). In 22 out of 28 MZ pairs both twins had the same type of EEG, a frequency of concord-

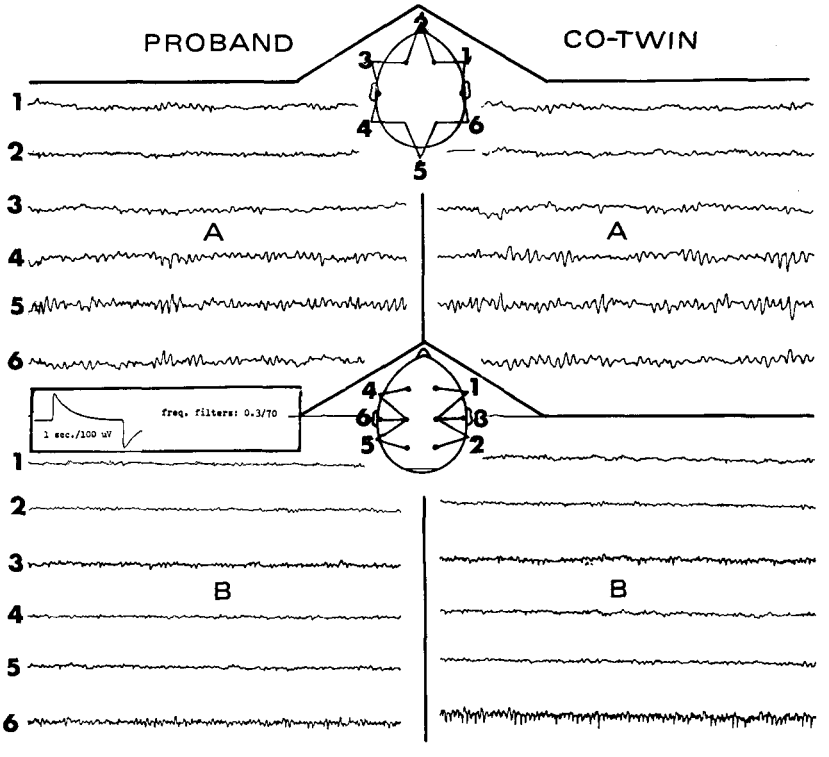

Fig. 1. *Twin pair A:* Age at follow-up: 23 years. Proband injury of 2nd grade two years earlier. No neurological signs. The proband was more neurasthenic and had lower intelligence capacity, but the co-twin was more aggressive.
EEG: The proband had lower alpha-percentage, more fast activity and his response on hyperventilation was more pronounced. The co-twin had slightly lower alpha frequency and voltage. Intra-pair difference (cf Tab. I): 6 points.
Twin pair B: Age at follow-up: 55 years. Proband injury of 2nd grade four years earlier. The proband was more antisocial, had lower intelligence and social position, but the co-twin was more neurasthenic and had more often headache.
EEG: The proband had lower alpha-frequency, but the co-twin had lower alpha-percentage, more slow activity and his hyperventilation response was more pronounced. Intra-pair difference: 10 points.

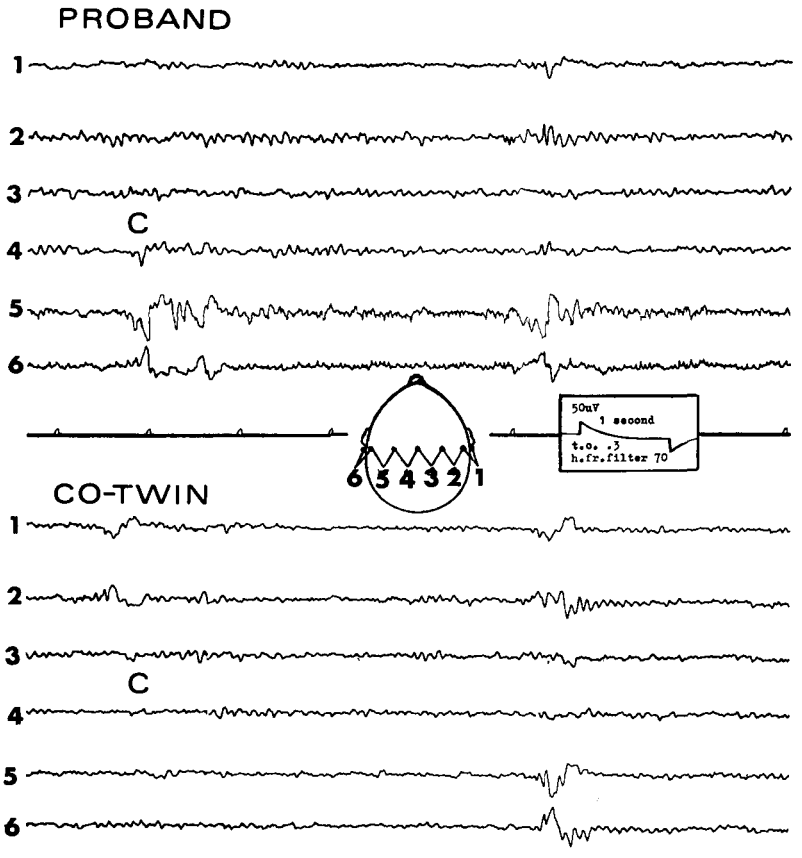

Fig. 2. *Twin pair C:* Age at follow-up: 11 years. Proband injury of 1st grade two years earlier. The proband was first born, had lower birth weight and probably had a birth injury. She was more neurotic and aggressive. There was no history of epilepsy in these twins.
EEG: The proband had lower alpha-frequency and more asymmetry in background activity. She had more of paroxysmal discharges, but the same kind of abnormality was found in the co-twin. Intra-pair difference: 11 points.

ance of 76%. In 16 of these pairs there were no abnormal findings, 2 pairs had slightly abnormal and 4 pairs moderately abnormal EEGs.

The analysis according to the point scale gave the scores shown in Tab. II. The probands showed in their EEGs a somewhat more pronounced tendency towards pathological aberrations than their partners. In 14 out of 28 pairs the brain-injured twins scored a larger sum of negative points than their co-twins. In 12 pairs, however, the scores were higher for the controls. There was no difference in 2 pairs.

The total sum of scores, expressing all aberrations and abnormalities in the records, was 122 points for probands against 90 for partners, which makes a mean

Tab. II. Scoring results according to the point scale *

Age at follow-up (years)	Intra-pair difference in points		
	Proband	Co-twin	Total
55	2	8	10
55	6	3	9
44	1	6	7
39	—	2	2
34	2	2	4
34	2	6	8
33	17	1	18
30	4	—	4
30	7	4	11
29	1	8	9
27	—	2	2
26	6	—	6
25	6	2	8
23	6	—	6
23	2	10	12
22	—	2	2
22	1	1	2
21	13	4	17
21	8	4	12
19	2	5	7
19	—	2	2
19	10	2	12
18	6	1	7
14	2	6	8
12	—	3	3
11	7	4	11
11	3	1	4
10	8	1	9
Sum of points	122	90	212

* The total for the 28 probands was 122 points against 90 for partners. This makes a mean value of 4.4 points for probands and 3.2 points for controls. The mean value for intra-pair difference, computed from all 28 pairs, is 7.6 points.

value of 4.4 points and 3.2 points respectively. The mean value for intra-pair difference, computed from all pairs, was 7.6 points. Correlated with the severity of the proband injury, corresponding means are given in Tab. III. The means of the total intra-pair differences seem to indicate a positive correlation with the severity of proband injury. The separate proband scores show, however, that there is no tendency to a correlation of this kind.

The next step was to find out if there were more significant associations between the EEG and some other factors, directly or indirectly connected to the proband

https://doi.org/10.1017/S1120962300012804 Published online by Cambridge University Press

injury. The factors investigated were: age at proband injury, the interval between head injury and follow-up, the signs of focal cerebral lesion immediately after the trauma and in follow-up, skull fracture, epilepsy and post-traumatic disability.

Time factors in connection with the head injury

Most of the proband injuries in this series occurred between the ages of 9 and 29 years. EEG at follow-up was more often abnormal in the twins with head trauma before 10 years of age (in 5 out of 9) than after it (6 out of 19). In the first group the probands with abnormal EEGs had a total score of 24 points (the mean per proband being 4.8) against the sum of 10 points for their co-twins (the mean being 2.0). In the second group the means were, respectively, 7.5 and 4.8 points.

Tab. III. Correlation between severity of proband injury and corresponding means from intra-pair differences according to the point scale *

Severity of proband injury (grade)	N. of pairs	Mean values of intra-pair difference		
		Probands	Co-twins	Total
1st	6	4.2	2.2	6.3
2nd	8	5.2	2.5	7.7
1st	6	4.2	2.2	6.3
2nd	8	5.2	2.5	7.7
3rd	6	4.5	3.7	8.2
4th	5	4.6	3.8	8.4
5th	2	2.0	4.0	6.0
6th	1	1.0	8.0	9.0

* The means of the total intra-pair difference seem to indicate a positive correlation with the severity of proband injury. The separate proband scores show, however, that there is no tendency to a correlation of this kind.

The mean interval between proband injury and follow-up was 4.5 years for the probands with abnormalities in the EEG, against a mean of 6.5 years for those who had normal or borderline records. This difference cannot be explained as a result of the proband injury, because there was practically no EEG difference between co-twins in pairs, where the injury/follow-up interval was less than 6 years. In this connection it is interesting to note that mean injury/follow-up interval for probands with EEG abnormalities was the same (4.5 years), whether the proband injury had occurred before or after 10 years of age.

https://doi.org/10.1017/S1120962300012804 Published online by Cambridge University Press

Signs of Cerebral Lesion and Skull Fracture

All the accidents were so-called closed head injuries. The acute neurological signs varied in severity from transient unconsciousness to focal abnormality such as anosmia, but there were no cases of paralytic or paretic symptoms. Symptoms of organic lesion persisted in only one proband, who had a bilateral and total anosmia. A skull fracture was found in 5 of 28 probands. There were no correlations between the EEG findings and the acute or late signs of cerebral lesion, or between the EEG and skull fractures.

Epilepsy

Two of the probands and one of the partners had convulsions when they were 1-3 years old. Another 3 had generalized convulsions immediately after birth. One of them was a proband who had a birth injury. The other two were partners with very low birth weights. All but one of the twins with epileptic symptoms, however, had already had their fits before their proband injuries.

Tab. IV. Pre- and perinatal conditions and EEG in 28 twin pairs *

Birth order, weight and *complications*	EEG more aberrant *or abnormal*	EEG less aberrant *or abnormal*
First born		
— proband	in 6 pairs	in 6 pairs
— partner	in 5 pairs	in 9 pairs
Higher birth weight		
— proband	in 7 pairs	in 7 pairs
— partner	in 3 pairs	in 5 pairs
Birth injury		
— proband	in 3 pairs	in 4 pairs
— partner	in 3 pairs	in 4 pairs

* None of these associative correlations showed in statistical analysis (χ^2) any differences reaching the 1% level of significance. However, 7 probands with higher birth weights than their co-twins had more abnormal EEG-records, but only 3 partners with higher birth weights had more marked EEG-abnormalities than their co-twins.

Post-traumatic disability

Among 22 probands with post-traumatic disability lasting less than 2 months there were as many normal as abnormal EEGs, 5 showing borderline findings. When the post-traumatic disability lasted 2-4 months, there were 2 normal and 3 abnormal EEGs. The only one who had not returned to full employment 6 months after his accident had a normal EEG.

Pre- and perinatal conditions

Because there were no statistically significant correlations between the EEG abnormalities and the proband head injuries, the question arose whether there was some other explanation of the differing EEG findings in probands and their co-twins, such as pre-and perinatal factors. During intra-uterine life twins may run a risk of differentiation by distribution differences in placento-umbilical blood supply. A brief analysis was made of possible correlations between EEG findings on one side and birth order, birth weight and birth complications on the other (Tab. IV). None of these associative correlations showed in statistical analysis (χ^2) any differences reaching the 1% level of significance. However, one observation is noteworthy: 7 probands with higher birth weights than their co-twins had more abnormal records, but only 3 partners with higher birth weights had more pronounced EEG abnormalities than their co-twins.

Discussion

The classical twin method aims at finding properties that are due to genetic factors by studying the intra-pair similarities and dissimilarities. In order to study how a brain injury affects the individual, MZ twins discordant for this factor have to be selected. Then, starting from intra-pair differences, one has to analyse relations between these differences on one side and the actual environmental factor on the other (Essen-Möller, 1957).

In one of the most exhaustive investigations of MZ twins (Vogel, 1958) a very high EEG concordance between healthy co-twins was found. In the present co-twin study the EEG differences between brain-injured twins and their MZ partners were very small, whether the EEG showed normal or abnormal patterns. This is a very important finding, for without the possibility to check by controls the causality of EEG abnormalities, these could have been taken for persisting traumatic signs after the proband injury. The risk of such a misjudgement would have been greater for a shorter interval between the accident and follow-up EEG than in the actual study. Abnormal EEGs would then be more expected and one would hesitate less to accept them as persisting signs of brain damage. Most traumatic EEG abnormalities are reversible in some days, weeks or months, depending on the severity of the brain injury. In the acute and subacute stage the amount of EEG abnormality is roughly proportional to the severity of the head injury (Denny-Brown, 1945; Steinmann and Tönnis, 1951). This correlation has been found to be present during the first six months after the head injury (Weber, 1954) but not afterwards (Greenblatt, 1943; Olsen and Rossen, 1950). Gibbs et al (1944) found that, following severe injuries, the percentage of abnormal EEGs continued to fall for as long as 2 years in the absence of epilepsy, while decrease was minimal in a group of post-traumatic epileptics. In general we agree with Cobb (1963), that the severity of the injury

dictates the degree of EEG change, though there are modifying factors, some of which are known, others obscure. If the severity of injury is judged from the existing state of consciousness, the abnormality tends to be greater in youth, in the presence of abnormal physical signs, with skull fractures and with open and penetrating wounds.

From the clinical point of view it is interesting that we have found in a MZ twin pair EEG abnormalities with identical patterns in identical regions (Fig. 2). This is an unusual but not unique finding. Barslund and Danielsen (1963) have described three pairs of MZ epileptic twins with temporal spike foci.

In the present study not only the head injured twins but also their partners showed a considerably greater incidence of abnormalities than is generally found in a randomly selected normal population. A similar observation was made by Lennox et al (1945), who found abnormal tracings in as many as 25% of normal twins as opposed to 15% of single-born normal persons. The difference between twins and single born is probably due to several factors, perhaps predominantly those concerning the pre- and perinatal conditions. Multiple pregnancy has many dangers, such as an increased incidence of toxaemia, abnormal presentations and placenta praevia. Dunn (1965) collected perinatal data prospectively on 358 twins among 4754 infants. The perinatal mortality for twins was 12.3%, or more than three times the average for all births.

In the conventional EEG analysis it is difficult to express quantitative differences between records with high similarity. The discrimination of the EEG was more effective by means of the point scale: an intra-pair difference of up to 5 points was scored although the records were entirely normal in both twins. The difference increased when the EEG showed pathological changes (maximum score of difference 18 points). In cases of concordant EEG abnormalities in co-twins, however, the score was in some pairs as low as 3-4 points. According to the scale there were only 2 twin pairs without any differences, and furthermore the brain-injured twins scored a larger sum of negative points than did their controls.

The results of this study indicate that twins with closed head injuries showed, in late follow-up, more aberrations and abnormalities of the EEG and that this intra-pair difference is associated with probandship, but fails to show any significant correlation with the proband injury. Nor was this difference related to pre- or perinatal factors.

The question then arises whether there were some hidden factors that disposed one of the co-twins to head injury and thus made him or her a proband? To answer this intricate question falls outside of this paper, but one of us has discussed these aspects on the basis of a larger twin material (Dencker, 1958, 1960, 1963). A statistical analysis of intra-pair differences showed that twins with pre-natal lesions were more easily fatigued than their co-twins; the ones with a higher birth weight were worse-tempered and more antisocial, while the ones with a lower birth weight had more anxiety symptoms. Birth order and birth complications were not associated with any intra-pair divergences. The results of different psychometric tests suggest that deficits shown by probands consisted mainly of reduction in cognitive functions,

such as ability for abstraction, perception and adaptation to an altered or unusual task. It should be noted, however, that the intelligence test did not discriminate. Nor did tests of concentration, fatigability and memory, which is interesting as such symptoms are usually reported in the post-traumatic cerebral syndrome.

Thus, neither differences in mental make-up nor in EEG characteristics has, in the present study, shown any statistically significant correlation with the severity of head injury. This observation limits the significance of EEG abnormalities in late concussional states. These abnormalities are probably more often of other genesis than traumatic. The results of this study, however, also indicate that there are *individually specific EEG patterns*, which in health retain their characteristics throughout different ages of the individuals. *As the physiognomy changes during maturation and aging, so changes the EEG, but both keep their special characteristics throughout life.* MZ twins are, from the genetic point of view, identical individuals and have the same EEG pattern. Thus, when a twin is influenced by a brain disease or lesion, the co-twin may serve as a biological control in both acute and follow-up studies.

Summary

A follow-up EEG study in 28 cases with closed head injuries, using MZ co-twins as controls, is described. A new concept in EEG analysis is introduced. A combined EEG code and point scale are more effective in discriminating subtle differences between two EEG records. A high concordance was found whether the EEG showed normal or abnormal patterns. Not only the head-injured twins but also the controls showed more abnormalities than in the normal population. Without this check by co-twins the EEG abnormalities could have been taken for persisting signs of the proband injury. It was found, however, in late follow-up that proband twins showed more EEG aberrations and abnormalities than co-twins, but the probands differed already in pre-traumatic mental make-up from their genetically identical controls. Neither differences in mental make-up nor in EEG characteristics showed any statistically significant correlation with the severity of the proband injury. These observations limit the significance of EEG abnormalities in late concussional states.

This study also indicates that there are individually specific EEG patterns, which in health retain their characteristics throughout life. The EEG pattern is therefore concordant in identical twins. Thus, when a twin is influenced by a brain disease or lesion, the co-twin may serve as a biological control in both acute and follow-up studies.

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RIASSUNTO

Vengono descritti gli EEG di 28 gemelli con traumi cranici, usando come controlli i cogemelli MZ. Viene introdotto un nuovo concetto nell'analisi EEG. Combinando il codice EEG ed una scala di punteggi, si riesce meglio a differenziare due EEG. È stata riscontrata un'elevata concordanza negli EEG sia normali che anormali. Non soltanto i gemelli con traumi, ma anche i controlli, presentavano più anormalità della popolazione generale. Senza questo controllo cogemellare, le anormalità EEG avrebbero potuto esser prese come segni persistenti del trauma. È stato riscontrato tuttavia, in un controllo successivo, che i probandi presentavano più alterazioni dei loro cogemelli, ma essi differivano, già prima del trauma, nella loro formazione mentale, dai loro cogemelli geneticamente identici. Né le differenze mentali, né quelle EEG presentavano una qualche correlazione significativa con la gravità del trauma. Tali osservazioni limitano il significato delle anormalità EEG in stadi avanzati posttraumatici. Tale studio indica anche l'esistenza di specifiche caratteristiche EEG individuali, che in condizioni di salute si mantengono inalterate per tutta la vita. Il tracciato EEG è quindi concordante nei gemelli identici; così, quando un gemello è influenzato da una malattia o lesione cerebrale, il cogemello può servire come controllo biologico, sia subito dopo il trauma che a distanza.

RÉSUMÉ

Les EEG de 28 jumeaux MZ, après traumatismes craniens, ont été comparés aux EEG de leurs partenaires indemnes. Un nouveau concept est introduit dans l'analyse EEG. Par une combinaison de côde et échelle de points, les deux EEG peuvent être mieux différenciés. Une concordance élevée a été remarqué dans les EEG normaux et anormaux. Non seulement les jumeaux traumatisés, mais aussi bien leurs partenaires, présentaient plus d'anomalies de la population générale. Sans ce contrôle gémellaire, ces anomalies auraient pu être mises en rapport aux traumatismes. Un contrôle successif a toutefois démontré plus d'anomalies chez les jumeaux atteints vis-à-vis des contrôles, mais leur formation mentale était déjà différente avant le traumatisme, nonobstant l'identité génétique. Ni les différences mentales, ni les différences des EEG, n'étaient significativement corrélées à l'entité du traumatisme. Ces observations réduisent l'importance des anomalies EEG en des stades post-traumatiques avancés. Cette étude indique aussi l'existence de caractéristiques EEG individuelles qui restent normalement inaltérées pour toute la vie. L'EEG est donc concordant chez les jumeaux identiques; ce qui fait que, si un jumeau est influencé par une maladie ou lésion cérebrale, son partenaire peut servir comme contrôle biologique, tout de suite après le traumatisme, ou bien après quelques temps.

ZUSAMMENFASSUNG

Beschreibung der EEG-Befunde von 28 Zwillingen mit Schädeltraumen unter Benutzung der jeweiligen EZ-Paarlinge als Kontrollen. Einführung eines neuen Konzepts in der EEG-Analyse. Bei Kombinierung des EEG-Kodixes mit einer Punktskala, lassen sich zwei EEG besser differenzieren. Sowohl in den normalen als in den anormalen EEG wurde eine grosse Konkordanz festgestellt. Nicht nur die mit Traumen behafteten Paarlinge, sondern auch die Kontrollpaarlinge wiesen mehr Anormalitäten als die allgemeine Bevölkerung auf. Ohne diese Paarlingskontrolle hätte man die EEG-Anormalitäten als weitere Anzeichen des Traumas gehalten. Bei einer Nachuntersuchung zeigte es sich allerdings, dass die Probanden mehr Alterationen als ihre Paarlinge aufwiesen, doch bestanden schon vor dem Trauma Unterschiede in der Geistesbildung zwischen den genetisch gleichen Zwillingen. Weder die geistigen nach die EEG-Unterschiede standen in irgendeinem wesentlichen Verhältnis zur Schwere des Traumas. Diese Beobachtungen beschränken die Bedeutung der anormalen EEG-Befunde bei fortgeschrittenen post-traumatischen Zuständen. Diese Untersuchung zeigt auch, dass es individuelle spezifische EEG-Merkmale gibt, die unter gesunden Verhältnissen das ganze Leben lang unverändert bleiben. Die EEG-Kurve ist demnach bei erbgleichen Zwillingen konkordant; auf diese Weise kann, wenn ein Zwilling von einer Gehirn — Krankheit oder — Läsion befallen wird, der andere Paarling sowohl nach dem Trauma als auch später als biologische Kontrolle dienen.