ELSEVIER

Electroencephalography and clinical Neurophysiology 98 (1996) 502–514

Genetic architecture of EEG power spectra in early life

G.C.M. Van Baal*, E.J.C. De Geus, D.I. Boomsma

Department of Psychophysiology, Vrije Universiteit, De Boelelaan 1111, 1081 HV Amsterdam, The Netherlands

Accepted for publication: 21 February 1996

Abstract

We measured the electroencephalogram (EEG) in 209 5 year old monozygotic (MZ) and dizygotic (DZ) twin pairs to estimate the relative contribution of genetic and environmental factors to EEG power spectra in early life. Data from same-sex and from opposite-sex twin pairs were used to test for sex differences in genetic influences. Results showed high concordance for EEGs of MZ twins for absolute and relative power in δ, θ, $\alpha 1$, $\alpha 2$, $\beta 1$ and $\beta 2$ bands. A model with additive genetic and unique environmental influences explained individual differences in both absolute and relative power in almost all bands and all electrode positions. Heritability of EEG power spectra was high. For absolute power the highest heritabilities were observed in θ, $\alpha 1$, $\alpha 2$ and $\beta 1$ power bands (mean heritability 81, 81, 78, and 73%, respectively). Somewhat lower heritabilities were found in δ and $\beta 2$ bands (mean heritability 55 and 64%, respectively). For relative power heritabilities were 63, 76, 71, 72, 68, and 65 for δ, θ, $\alpha 1$, $\alpha 2$, $\beta 1$, and $\beta 2$, respectively. Virtually no sex differences in heritability were found. These findings indicate that the background EEG is one of the most heritable characteristics in early life.

Keywords: Electroencephalogram; Power spectra; Children; Heritability; Twins

1. Introduction

Most of the salient changes in brain anatomy take place in the first 4 years of life, for example growth in brain weight (Blinkov and Glezer, 1968), increased myelination (Yakovlev and Lecours, 1967), glucose utilization (Chugani et al., 1987), and synaptic growth (Huttenlocher, 1979). Many major developmental changes in behavior occur in the period of 4–6 years (Thatcher et al., 1987). It has been suggested that these changes coincide with anatomical changes that are less 'massive' than those during the first years, but greatly improve functional connectivity of the various parts of the brain. Among these are selective death of irrelevant synapses and strengthening of the relevant ones (Goldman-Rakic, 1987; Nowakowski, 1987) and myelination of fibers in integrative cortical interhemispheric and intrahemispheric connections (Courchesne, 1990). Electroencephalogram (EEG) activity has been proposed as a non-invasive index of these developmental changes. This is a study of the relative importance of genetic and environmental influences on the electrical brain activity in a group of 5 year old children.

Spectral analysis (Fourier analysis) can be used to determine the amount of variance in the EEG signal explained by cyclic components with a certain frequency ('power', in Hz). Several studies have shown strong developmental changes in EEG power (Matoušek and Petersén, 1973; Chavance and Samson-Dollfus, 1978; Samson-Dollfus and Goldberg, 1979; John et al., 1980; Matthis et al., 1980; Katada et al., 1981; Benninger et al., 1984; Gasser et al., 1988). These studies all show the same basic tenet: slow activity is dominant in early life, but is substituted by faster activity with increasing age. As the child gets older, total power in the low frequency bands (δ, θ and α) decreases, whereas total power in the higher (β) bands stays constant. Various studies suggest that, in addition to gradual changes, discrete growth spurts in EEG spectra may be found (Thatcher et al., 1987) that may be linked to stage transitions in cognitive development (Hudspeth and Pribram, 1992; Thatcher, 1994). In spite of these overall trends, individual differences in EEG power in children of the same age are striking (Ben-

* Corresponding author. Tel.: +31 20 4448802; fax: +31 20 4448832; e-mail: caroline@psy.vu.nl.

0013-4694/96/$15.00
PII S0304-3940(96)95601-9

EEG 95601

ninger et al., 1984). These individual differences are increasingly being used to diagnose deviant brain development, such as that related to neurological and behavioral problems like dyslexia and hyperactivity (John, 1989). The determinants of such individual differences in children's EEG are largely unknown. It is likely that genetic factors play a major role. Evidence suggests that approximately 30% of the entire genome is expressed only in the brain (Sutcliffe and Milner, 1984), which is much more than in any other tissue.

In adults, a number of studies of genetic and environmental influences on EEG parameters have been conduct ed (for a review, see Van Beijsterveldt and Boomsma, 1994). Most of these studies used the twin method to estimate the relative influences of genes (heritability) and environment on individual differences in the EEG. The twin method is based on the fact that identical or mono zygotic (MZ) twins share all their genes, whereas fraternal or dizygotic (DZ) twins only share 50% of their genetic material on average. Heritability (h^2) can be estimated as twice the difference between the MZ correlation and the DZ correlation: $h^2 = 2(r\text{MZ} - r\text{DZ})$, or by model fitting techniques (Boomsma and Gabrielli, 1985). In most earlier studies only small samples were available, and no formal model fitting methods were used to estimate genetic and environmental influences. Sex differences in genetic and environmental influences on EEG were ignored, and although EEG changes significantly with age, most studies used wide age ranges with virtually no children. In spite of the methodological pitfalls, all adult studies have reported the robust finding of high to very high genetic contribution to individual differences in the EEG power spectra of adults.

We cannot assume that the genetic architecture of CNS functioning is the same in infants, older children and adults. Particularly in children, it is possible that there may be periods during development in which brain functioning is more sensitive to environmental influences than to genetic factors and vice versa. An example of changing heritability with age is provided by intelligence: heritability of IQ increases from about 15% at infancy to about 50% at older ages (Boomsma, 1993). A few of the EEG studies in twins included in addition to adults some children (Vogel, 1958; Dumermuth, 1968; Whitton et al., 1985). However, the age ranges in these studies were too large, or the number of subjects too small to draw conclusions about the differential heritability of children and adult EEGs.

In this study we specifically address the genetic and environmental sources of individual differences in the EEG power spectrum of 5 year old children, in a period of increased cortico-cortical connectivity. The sample included male and female same-sex MZ and DZ twins to test for sex differences in heritabilities, as well as twins of opposite-sex to look at the question whether the same genetic factor is expressed in males and females.

2. Methods

2.1. Subjects

This study is part of a larger project in which genetic and environmental influences on neural development in early life are studied longitudinally. Healthy Dutch 5 year old twin pairs ($n = 209$; mean age 5.26 years, SD 0.19) participated. All subjects had normal or corrected to normal vision. Addresses of the twin pairs were obtained from the Netherlands Twin Register, which registers between 45 and 50% of all Dutch twins born after 1986 (Boomsma et al., 1992). For 103 same-sex twins zygosity was determined by blood typing (ABO, MNS, Rhesus, Kell, Duffy, Kidd, Lutheran). Parents of all same-sex twin pairs ($n = 170$) completed a zygosity questionnaire (Goldsmith, 1991), and discriminant analysis was used to determine zygosity of the twins for whom no blood typing was available. All multiple choice questions (19) entered the analysis, but only 4 questions (hair color, hair structure, confusion by acquaintances, confusion by close friends of the family) remained which discriminated best between MZ and DZ twins. In the group of 103 same-sex twins already classified by blood typing, 95% was classified correctly; no actual MZ twins were classified DZ, and 5 DZ twins were classified as MZ.

Eighteen twin pairs had incomplete EEG data because of difficulties during the experiment. Children who fell asleep during the experiment (11), and children who showed high level of arousal or cried (13) were also excluded from further analyses. This left 167 twin pairs (monozygotic males (MZM), 34; dizygotic males (DZM), 33; monozygotic females (MZF), 37; dizygotic females (DZF), 32; dizygotic opposite-sex twins (DOS), 31) with complete data.

2.2. Procedure

Twins were measured on the same time of day (morning or afternoon). After arrival in the laboratory the protocol was explained to the twins and their parents. Height, weight and head circumference were measured. One of the twins started with the EEG/ERP experiment, the other twin was given an IQ test (Boomsma and Van Baal, in preparation). While the child watched a video, an electrocap with electrodes in the 10–20 system of Jasper (1958) was attached. Electrode impedance was kept below 10 kΩ. Four tin electrodes for eye movement recordings, two ear electrodes as references and one tin electrode for an electrocardiogram were also attached. Testing took place in a dimly lit, electrically shielded, sound attenuated cabin with intercom facilities. Subjects lay on a bed with a black and white 25 × 30 cm monitor about 50 cm above their heads. One parent was allowed to stay with the child. The experimental conditions consisted of an auditory habituation task, a visual oddball task and 6 min

of quiet rest (3 min eyes open, 3 min eyes closed). In this paper data of the background EEG measured during quiet rest with eyes closed are presented.

2.3. Apparatus

EEG was recorded continuously on an 18 channel Nihon Kohden PV-441A polygraph. Time constants were set to 5 s, and high frequency cut-off was 35 Hz and sample frequency was 250 Hz. Signals were converted with a 12 bits AD converter, and sent to an Olivetti M28 PC for offline processing.

2.4. Data quantification and data reduction

EEG was measured at the following scalp locations: prefrontal (Fp1, Fp2), frontal (F7, F3, F4, F8), central (C3, C4), parietal (P3, P4), occipital (O1, O2) and temporal (T5, T6). Linked earlobes were used as references according to the method described in Pivik et al. (1993). Briefly, we used two separate preamplifiers with high input impedance for each of the reference electrodes and linked the output electrically. Calibration showed highly comparable gain and accuracy range of the two preamplifiers. With the ears linked this way the effects of possible imbalances in electrode impedance introduced by the electrical double layers were prevented. Vertical eye movements were measured at infra and supra orbital sites in line with the pupil of the left eye (VEOG), and horizontal eye movements at the outer canthuses (HEOG).

Single trial EOG artifacts were removed using dynamic regression in the frequency domain (Brillinger, 1975), and the EEG signal was divided into 90 2 s epochs. Epochs with clippings were automatically excluded from further analysis. During visual inspection, epochs with abnormal EEG patterns (like ECG artifacts, movement artifacts) were noted in the protocol, and removed from the analyses. For every epoch and for every scalp location the raw EEG was then converted from the time domain into the frequency domain using Fast Fourier Transformation (FFT). This procedure yields a power spectrum for every individual, which indicates for every cyclic component how much variance in the raw signal is accounted for by this component. The power spectra, ranging from 0.5 to 30 Hz, with a resolution of 0.5 Hz, were averaged over all epochs without artifacts (never less than 20) to obtain the average power spectrum for all 14 electrode positions. From these power spectra both absolute and relative power of more traditional broad bands per scalp location were calculated: absolute power is the sum of power in a certain frequency range, relative power is the absolute power in that band divided by the sum of all power bands in the EEG. We defined 6 different bands: δ is the sum of power in the frequency bands ranging from 1.5 to 3.5 Hz, θ ranged from 4.0 to 7.5, $\alpha 1$ from 8.0 to 9.5, $\alpha 2$ from 10.0 to 12.5, $\beta 1$ from 13.0 to 17.5 and $\beta 2$ from 18.0 to 25.0 Hz. To obtain a normal distribution of the data 10-log transformations were conducted on absolute values, and logit transformation (i.e. $10\text{-log}(x/1-x)$) for relative powers.

2.5. Statistical analysis

In a simple one-way analysis of variance we first tested for birth order effects, e.g. differences between firstborn and secondborn twins, in mean values of absolute and relative δ, θ, $\alpha 1$, $\alpha 2$, $\beta 1$ and $\beta 2$ power. We then tested for differences in EEG powers between zygosities (MZ and DZ), sexes (male and female), and electrode positions (Fp1, Fp2, F7, F3, F4, F8, C3, C4, T5, P3, P4, T6, O1 and O2) using multivariate analyses of variance (MANOVA, SPSSPC). Analyses were conducted separately for twin A (firstborn child) and twin B (secondborn child) of the twin pair, because, due to their genetic relatedness, their data are not independent. Testing for differences between zygosities is essential because an assumption of the twin design is that monozygotic and dizygotic twins all stem from the same population, and therefore will show no differences in means and variances.

Secondly, to obtain an indication of measurement error, we computed split-half reliabilities using power spectra averaged over all odd, and over all even 2 s epochs from the total EEG registrations, for all leads and frequency bands separately.

The final class of analyses decomposed the observed variance in the EEG power into genetic and environmental factors, using structural equation modeling with the computer program Mx (Neale, 1994). With structural equation modeling, a model is constructed which specifies causal relationships between the observed phenotype, in our case the EEG variables, and the unobserved genetic and environmental factors influencing the phenotype. Genetic factors are the sum of small effects of many genes. Two sorts of effects are possible for each of these genes: additive genetic effects in which the effects of the paternal and maternal alleles are added up, and dominance effects, in which the paternal or maternal allele is dominant for some of the genes. In the environmental factors, a distinction can be made between common environmental influences and unique environmental influences. Common environmental influences are shared by relatives growing up in the same family, for instance food habits, or going to the same school. Non shared, or unique environmental influences cause differences between cotwins even if they have the same genotype and live in the same family. These include measurement errors (Plomin et al., 1990; Neale and Cardon, 1992).

The basis for structural modeling in twin studies is the different level of genetic relatedness in monozygotic (MZ) and dizygotic twins (DZ) in combination with a similar common environment. Fig. 1 shows a path diagram of a structural model in which the observed pheno-

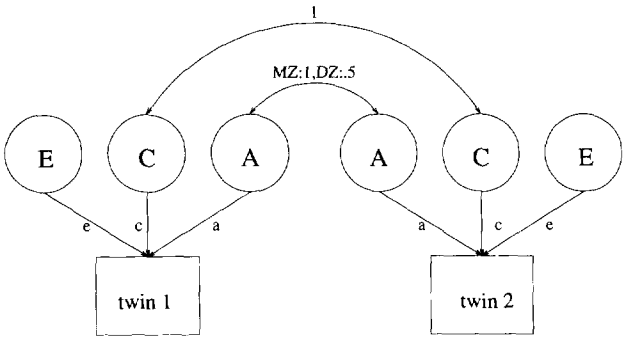

Fig. 1. Path diagram of a univariate twin model. Phenotypes of both twins (twin 1 and twin 2) are influenced by additive genetic factors (A), common environmental factors (C), and unique environmental factors (E). Correlation between C_{twin1} and C_{twin2} is 1, correlation between A_{twin1} and A_{twin2} is 1 for MZ twins and 0.5 for DZ twins.

type (P: measured in twin 1 and twin 2) is influenced by an additive genetic factor (A), a shared common environmental factor (C) and a non shared unique environmental factor (E): P = A + C + E.

Since MZ twins share all their genes and DZ twins share 50% on average, the correlation between additive genetic factors (A) is set to 1 for MZ twins, and to 0.5 for DZ twins. The common environmental correlation is 1 in both MZ and DZ twins. Correlations for the non shared, unique environmental influences (E) are set to 0 for both types of twins. Dominance genetic effects were not included in the model, because twin correlations did not give an indication for such effects. It is only of importance if DZ correlations are close to 25% of the MZ correlations. Furthermore, dominance for polygenetic traits is difficult to estimate in a twin model.

The model outlined in Fig. 1 will be tested against the observed EEG data. The aim is to find the most parsimonious model which still adequately describes the data. Estimates of the genetic, common environmental and unique environmental factors are obtained from the observed variance. These are the parameters a, c and e, respectively.

In Fig. 1, we have not accounted for possible sex differences in the relative influence of genetic and environmental effects. It is possible to account for such differences, particularly when DZ opposite sex twins are available. Sex differences can be estimated in three different models (Neale and Cardon, 1992):

(1) Scalar effects sex-limitation models, in which a difference in total variance between males and females is allowed, but in which the relative contributions of A, C and E are the same for males and females;
(2) Common effects sex-limitation models. In these models the relative magnitude of genetic and environmental factors can differ between the sexes, but the same genes and/or common environmental influences are expressed;
(3) General sex-limitation models. These test the possibility that sex specific genes exist, which influence the trait in one sex but not in the other. For these models the DOS twins are essential.

When the same genes explain part of the variance in both males and females, but their relative contributions differ, then the additive genetic correlation in DOS pairs is 0.5. When different genes account for the phenotypic variance the additive genetic correlation in DOS pairs will be smaller than 0.5, or even 0, and the observed correlation in DOS pairs will be smaller than in same-sex pairs.

Data on male and female same-sex MZ and DZ twins and on DZ opposite-sex twins were summarized into 5 2×2 variance-covariance matrices. The diagonal elements of the matrices give the variances of the phenotypes for first- and second-born twins, and the covariance between twins is given in the off-diagonal elements. The models outlined above were fitted to these matrices, such that the most parsimonious model remained. The most parsimonious model is the model with most degrees of freedom (i.e. least parameters necessary to describe the data), which is not significantly worse in describing observed variance-covariance matrices than a model with more parameters. The values of the parameters a, c and e were estimated by maximum likelihood. When the observed variances and covariances deviate only slightly from the variances and covariances as predicted by the model, the model will show a good fit. The fit between the observed data and the model was assessed by χ^2 tests. A low χ^2 and a high P-value indicate a good fit of the model to the observed data. To compare the fit of two different models, hierarchic χ^2 tests are used. The hierarchic χ^2 is the difference between the χ^2 of a model and the χ^2 of a reduced form of that model (e.g. from a full scalar ACE model to a full scalar AE model). Heritability (h^2) is the proportion of observed, phenotypic variance that can be explained by the genetic factor, and is equal to $a^2/(a^2 + c^2 + e^2)$. Likewise, common environmentability (c^2) is the proportion of observed, phenotypic variance that can be explained by the common environment factor, and is equal to $c^2/(a^2 + c^2 + e^2)$, and unique environmentability (e^2) is the proportion of observed, phenotypic variance that can be explained by the unique environment factor ($e^2/(a^2 + c^2 + e^2)$).

3. Results

Fig. 2 shows the power spectra for each electrode position. In 5 year old children slow waves dominate. The sum of δ, θ and $\alpha 1$ activity explains 84–92% of total variance in the signal, whereas faster waves (i.e. $\alpha 2$, $\beta 1$ and $\beta 2$) explain only 8–16% of the variance in the EEG during rest.

Most power was found in the lowest frequency band (δ). On posterior scalp locations, power in θ, $\alpha 1$ and $\alpha 2$ bands was larger than on anterior scalp locations and a

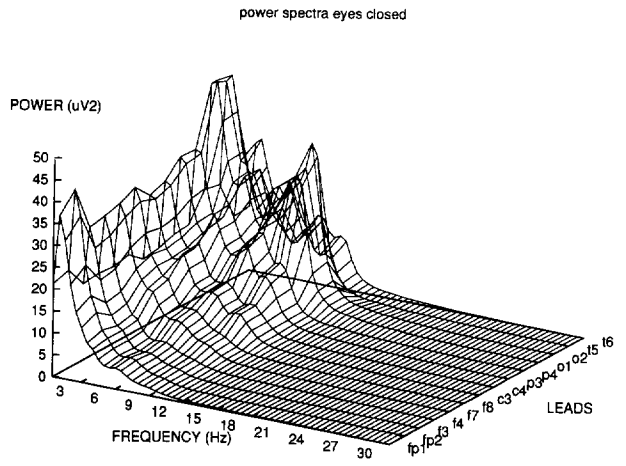

Fig. 2. Power spectra averaged over all subjects during rest with eyes closed for 14 electrode positions, from 0.5 to 30 Hz with a resolution of 0.5 Hz. Plotted are absolute, non transformed values. Most power is found in the δ band. On occipital leads a clear peak in the $\alpha 1$ band at 8.5 Hz is found.

peak was found at frequency 8.5 Hz on occipital scalp locations. Powers in the $\beta 1$ and $\beta 2$ bands were small but significantly different from zero. Mean EEG powers of firstborn twins were not significantly different from those of the secondborn twins at any scalp location in any band. Multivariate analysis of variance of both absolute and relative power showed no differences between zygosities for power in all frequency bands. No sex differences were found for mean absolute δ, θ and $\alpha 1$ power, but females had slightly higher absolute powers in $\alpha 2$, $\beta 1$ and $\beta 2$ bands. For relative power, sex differences were significant in $\alpha 2$ and $\beta 1$ band: relative power was larger in females. Mean differences for electrode positions were highly significant. Absolute power was highest at posterior scalp locations, except $\beta 2$ power, which was highest at frontal leads. Relative power was higher on anterior leads than on posterior leads for δ, $\beta 1$ and $\beta 2$ band. For θ, $\alpha 1$ and $\alpha 2$ band relative power was higher on posterior than on anterior leads. A summary of multivariate analyses of variance with sex, zygosity and electrode position as independent variables is shown in Table 1.

Split-half reliabilities for absolute and relative power in the 6 broadbands were unanimously high. No differences between electrode locations were found, and average reliabilities were computed across all electrodes for each of the 6 frequency bands. Split-half reliabilities for absolute power were 0.89, 0.96, 0.96, 0.96, 0.95 and 0.93 for δ, θ, $\alpha 1$, $\alpha 2$, $\beta 1$ and $\beta 2$, respectively. For relative power the reliabilities were 0.88, 0.91, 0.92, 0.92, 0.90 and 0.92, respectively.

3.1. Genetic analyses

As a first step, MZ and DZ correlations were computed on absolute and relative powers of all bands and all leads (Appendix A). These correlations give an indication of which factors influence the trait. When MZ correlations are twice the DZ correlations, genetic factors are important. When MZ and DZ correlations are equal (but not

Table 1

F-values of multivariate analyses of variance with independent variables sex (male or female), zygosity (MZ or DZ), electrode position (Fp1, Fp2, F7, F3, F4, F8, C3, C4, T5, P3, P4, T6, O1 or O2) and interaction effects of sex × zygosity (s × z), zygosity × electrode position (z × e), sex × electrode position (s × e), and sex × zygosity × electrode position (s × z × e)

	df	δ	θ	$\alpha 1$	$\alpha 2$	$\beta 1$	$\beta 2$
Absolute power							
Sex	1163	<1	<1	3.57	5.04*	11.47*	6.36*
Zygosity	1163	<1	<1	<1	1.22	1.81	<1
Electrode	13151	63.09*	213.06*	308.06*	187.92*	102.59*	32.68*
s × z	13151	1.23	<1	<1	<1	<1	<1
s × e	13151	1.46	1.71	<1	<1	1.76	1.44
z × e	13151	1.11	1.25	<1	<1	<1	1.02
s × z × e	13151	<1	<1	<1	<1	<1	<1
Relative power							
Sex	1163	2.92	<1	3.82	4.36*	11.70*	3.06
Zygosity	1163	<1	<1	<1	<1	<1	<1
Electrode	13151	89.01*	69.48*	74.73*	46.82*	40.48*	108.52*
s × z	13151	<1	<1	<1	<1	<1	<1
s × e	13151	1.81*	1.62	2.25*	1.13	<1	<1
z × e	13151	<1	<1	<1	1.77	1.33	1.54
s × z × e	13151	<1	<1	<1	<1	<1	<1

Table shows results of twin A only.

*$P < 0.05$. Significant *F*-values, df = 1163: 3.90 for $\alpha = 0.05$ and 6.79 for $\alpha = 0.01$; significant *F*-values, df = 13 151: 1.79 for $\alpha = 0.05$ and 2.25 for $\alpha = 0.01$.

Table 2
Best fitting models and their χ^2

Electrode	δ		θ		$\alpha 1$		$\alpha 2$		$\beta 1$		$\beta 2$	
	Model	χ^2	Model	χ^2	Model	χ^2	Model	χ^2	Model	χ^2	Model	χ^2
Absolute power												
Fp1	AE***	8.96	AE***	8.36	AEsx**	12.84	AEsx**	11.30	AE	23.94	AE*	20.73
Fp2	AE***	6.58	AE**	9.86	AEsx***	5.97	AEsc***	7.92	AEsc**	13.95	AE**	14.37
F7	AEsx*	16.61	AE**	15.46	AE*	16.32	AE**	9.54	AE**	13.09	AEsc**	14.08
F3	AE***	7.13	AE**	14.72	AE**	13.75	AE**	9.72	AE*	18.29	AE**	12.60
F4	AE**	13.72	AE*	18.45	AE***	9.12	AEsc***	7.13	AEsc**	14.22	AE**	11.10
F8	AE*	21.39	AE***	8.88	AE***	5.52	AE**	11.81	AE**	9.90	AE**	10.10
C3	AE*	21.62	AE**	15.46	AE**	12.67	AEsx**	9.05	AE*	19.91	AE**	15.19
C4	AE*	20.56	AE*	19.08	AE**	10.84	AEsx***	5.34	AE	26.78	AE*	17.82
T5	AE*	18.97	AE**	12.07	AE*	18.87	AE***	7.75	AE**	15.81	AE**	15.30
P3	AE	33.63	AE**	9.39	AE***	8.71	AE***	6.33	AE**	13.52	AE**	13.89
P4	AE	24.20	AE**	10.98	AE***	6.17	AE***	5.64	AE*	18.40	AE**	10.59
T6	AE*	19.62	AE***	6.17	AE*	18.82	AE**	14.04	AE**	11.12	AE**	10.50
O1	AE*	18.74	AE***	8.53	AE*	18.14	AE**	9.36	AE**	11.78	AE**	11.84
O2	AE	24.31	AE***	6.80	AE**	12.92	AE[a],**	15.09	AE***	9.28	AE**	11.75
Relative power												
Fp1	AE***	6.33	AE**	10.72	AE**	12.92	AE*	18.82	AE**	12.19	AE**	12.28
Fp2	AE***	6.13	AE**	14.99	AE**	14.67	AEsc*	18.79	AE**	12.64	AE**	11.00
F7	AEsx*	14.41	AEsx*	15.88	AEsx***	6.78	AEsx**	8.08	AEsx***	5.88	AEsc***	7.60
F3	AE**	14.36	AE**	14.75	AE***	7.51	AE**	14.06	AEsx***	5.23	AE***	3.60
F4	AE*	16.55	AE*	18.07	AE***	7.70	AE**	15.72	AE*	16.67	AE**	12.16
F8	AE*	21.84	AE	23.11	AE*	19.55	AE**	15.99	AEsx**	8.24	AE**	11.17
C3	AE**	13.64	AE***	5.19	AE***	8.94	AE**	15.87	AEsx**	15.86	AE***	7.11
C4	AE*	19.70	AE**	14.93	AE**	10.53	AEsx**	8.18	AEsc**	17.54	AE**	9.78
T5	AE*	17.22	AE***	5.03	AE**	12.27	AE**	11.21	AE***	5.68	AEsc***	7.29
P3	AE	23.47	AE***	9.16	AE***	9.15	AEsx**	8.55	AE**	10.48	AE***	4.98
P4	AE***	8.62	AE***	7.11	AE***	5.51	AE**	15.04	AE**	12.11	AE***	7.77
T6	AE**	11.62	AE***	7.89	AE***	6.57	AE***	6.55	AE**	12.68	AE***	7.06
O1	AE**	14.55	AE**	11.45	AE**	11.62	AE**	14.28	AE**	13.52	AE**	9.50
O2	AEsx**	9.17	AE**	12.97	AE***	6.43	AE*	20.69	AE*	16.10	AE***	8.97

Models containing additive genetic and unique environmental factors without sex differences (AE) have 13 degrees of freedom (df), scalar models (AEsc) have 12 df, and models with non-scalar sex differences (AEsx) have 11 df. Probability of the models: $*P > 0.05$, $**P > 0.25$ and $***P > 0.75$.
[a]Including a common environment factor gave a slightly better fit.

zero), common environment is of importance. There is a large concordance between children from the same family for both absolute and relative power. For all electrode positions and all bands correlations of MZ twins with their cotwins are very high, and correlations of same-sex DZ twins with their cotwins are about half the MZ correlations. Correlations of the male-female DOS twins with their cotwins are about the same as the DZ same-sex correlations, indicating that the same genetic and/or environmental influences are expressed in boys and girls.

Whether the influences of genetic and common environmental factors on the EEG powers are significant can be tested using structural equation modeling. Model fitting showed that the variance in the data was best explained by models containing additive genetic and unique environmental factors. Large heritabilities were found for absolute and relative power in almost all bands and electrode positions. We further tested for influences of common environment, which would cause both MZ and DZ twins to be more alike, but this factor hardly ever was significant for any band or electrode position. The most parsimonious models were, therefore, models with additive genetic and unique environmental factors only (AE models), as is shown in Table 2.

For almost all EEG powers on all scalp locations heritabilities were the same for males and females. A scalar sex-limitations model, in which the total variance was allowed to differ between males and females, but the relative contributions of genes and environment is the same, gave a better fit to the data in some cases. In these models variance was always larger in males than in females. A common sex-limitations model was found a few times. Frontal lateral left electrode position (F7) showed larger heritabilities of absolute power in females for δ power at F7. As a consequence, higher heritabilities in females were found for relative powers on that same location. Heritabilities of absolute α power were higher in females at prefrontal scalp locations, and higher in males

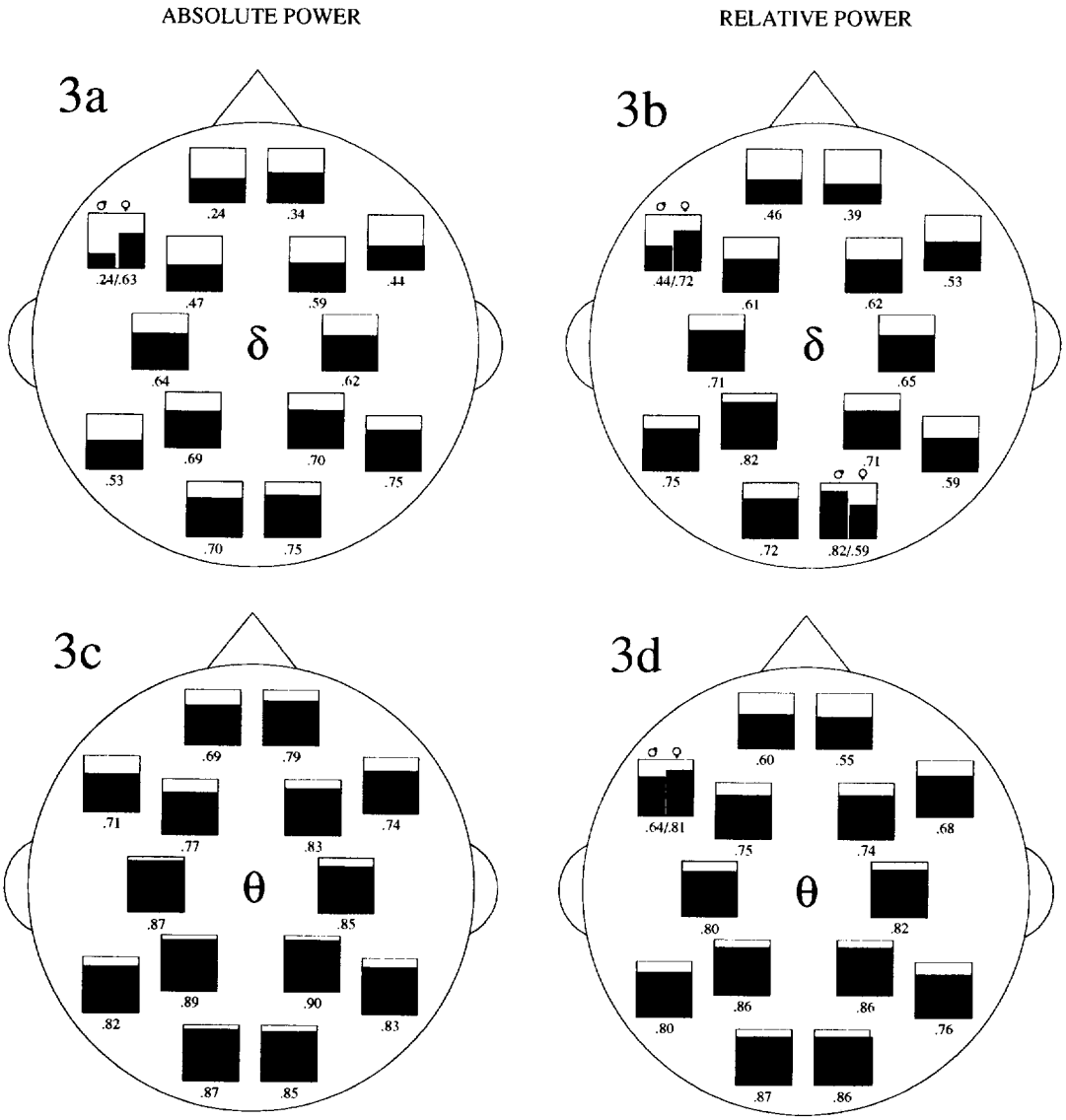

Fig. 3. (a–d) Heritabilities of absolute and relative δ (a,b) and θ (c,d) power, during rest with eyes closed.

at central scalp locations ($\alpha 2$). These sex differences are scant and show no obvious systematic pattern. In all instances, the same genetic factor always influenced the observed trait in both sexes, since a general sex-limitations model was never the best fitting model. For the largest part of our data, therefore, the most parsimonious models were AE models without sex differences. Figs. 3, 4 and 5 display the heritabilities for absolute and relative power for 6 bands and 14 electrodes for the best fitting models.

With regard to the success of model fitting: for absolute power these models fitted the data well in θ, $\alpha 1$ and $\alpha 2$ bands, with 29% of the models showing a probability of more than 0.75 that the data were described correctly by the model. Eighty-nine percent of the models showed a probability of more than 0.25. For β bands 66% of the models showed a probability of more than 0.25, but for δ band this was only 32%, indicating that the lower heritabilities of absolute power in the δ band must be interpreted with some caution. For relative power the AE models fitted the data extremely well in all bands, with a moderate exception of relative δ power. Thirty-six percent of the models showed a probability of more than 0.75 that the data were described correctly by the model; 87% of the models showed a probability of more than 0.25.

Heritabilities in θ, $\alpha 1$ and $\alpha 2$ bands were extremely high, with mean heritabilities of absolute power of 81%, 81% and 78%, respectively. Heritability also explained a large part of the individual differences in absolute power in the δ and β bands, particularly in the occipital and parietal leads. Mean heritabilities were 55%, 73% and 64%, respectively.

Heritabilities of relative power were high in all bands,

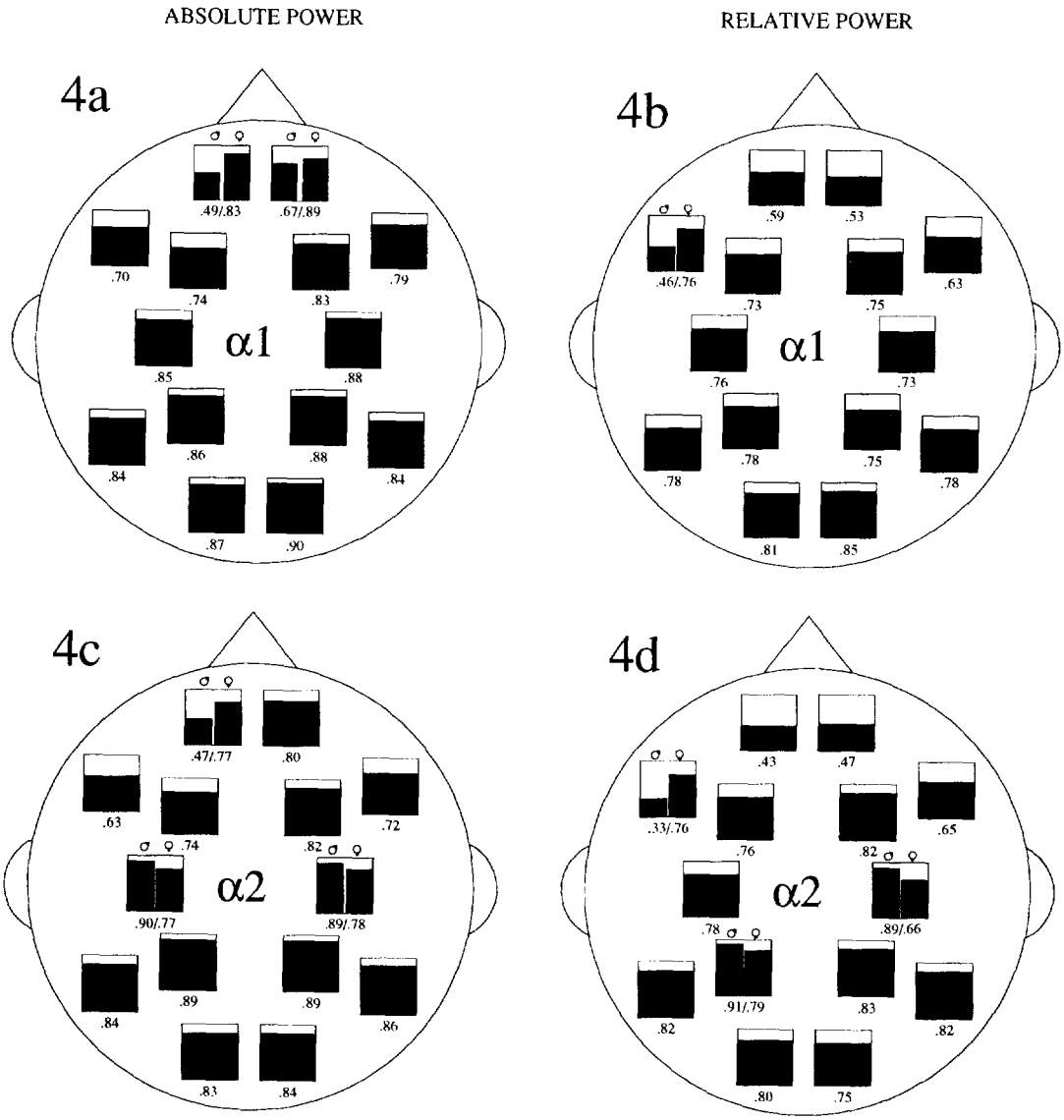

Fig. 4. (a–d) Heritabilities of absolute and relative $\alpha 1$ (a,b) and $\alpha 2$ (c,d) power, during rest with eyes closed.

with a mean heritability of 63%, 76%, 71%, 72%, 68%, and 65% for relative δ, θ, $\alpha 1$, $\alpha 2$, $\beta 1$ and $\beta 2$ power, respectively.

In our models no explicit multivariate testing of electrode location was performed. However, according to the 95% confidence intervals, heritabilities for both absolute and relative power in all bands decreased significantly from anterior to anterior leads. No significant differences in heritabilities were found between homologous electrodes at left and right hemispheres. The 95% confidence intervals are 21–56% for $h^2 = 40\%$, 33–64% for $h^2 = 50\%$, 45–71% for $h^2 = 60\%$, 58–79% for $h^2 = 70\%$, 71–86% for $h^2 = 80\%$, and 85–93% for $h^2 = 90\%$. Some caution is in order in interpreting inter-regional comparisons, since they may be slightly confounded by different contributions of common activity coming from the linked ears reference.

4. Discussion

The objective of the present study was to determine the genetic architecture of electrical brain activity in 5 year old children. In short, the results are that nearly all EEG power spectra measures are highly heritable, and that heritabilities were nearly always the same for boys and girls. Heritabilities of EEG power were slightly higher at posterior than at anterior scalp locations, but no differences were found between left and right hemispheres.

On visual inspection, the dominant picture found in the EEG of 5 year olds usually is that of posterior α, frequently interrupted by intermingled slow waves, mostly in the range of 1.5–4 Hz, extending from occipital into the posterior temporal and, less impressively, into the parietal regions (Niedermeyer and Lopes da Silva, 1993). Frequency analysis in our twins generally confirmed this

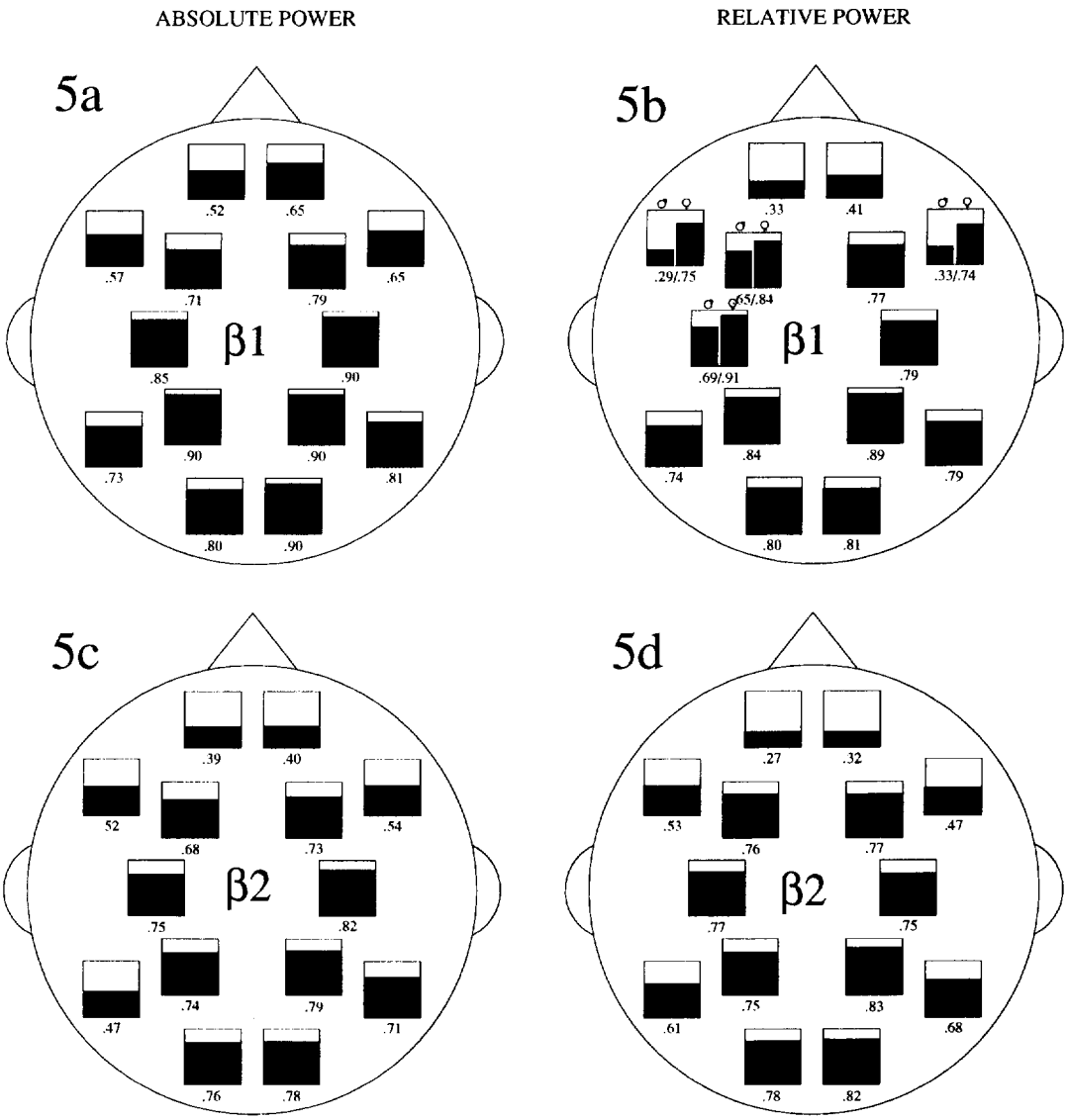

Fig. 5. (a–d) Heritabilities of absolute and relative $\beta 1$ (a,b) and $\beta 2$ (c,d) power, during rest with eyes closed.

pattern. Delta contributed strongly to power on all leads with a peak in the posterior leads. Power in the α and θ bands were also high throughout, except for the frontal leads. Although activity of the low voltage $\beta 1$ and $\beta 2$ contributed only little to the total power, it was present in virtually all children and, as in the other bands, large individual differences were found. The absolute values for EEG powers found in this study, referenced to linked ears, correspond well to power values reported previously (Gasser et al., 1988) and to mean amplitudes (i.e. square root of power) reported from visual scoring (Niedermeyer and Lopes da Silva, 1993).

Small but significant mean differences between boys and girls were found for absolute $\alpha 2$ and β power, and for relative $\alpha 2$ and $\beta 1$ power. Girls had higher absolute $\alpha 2$, $\beta 1$ and $\beta 2$ power and higher relative $\alpha 2$ and $\beta 1$ power than boys in all leads. This contrasts with the results of others. Some studies did not find significant sex differences in EEG amplitudes (Matoušek and Petersén, 1973; Gasser et al., 1988). Other studies (Matthis et al., 1980; Benninger et al., 1984) showed higher relative $\alpha 1$ and $\alpha 2$ in boys and higher relative θ in girls below the age of 6. However, our results do agree with Petersén and Eeg-Olofsson (1971) who, using visual analysis, found higher α frequencies in girls compared with boys up to 11 years of age. Since girls are more advanced with regard to many biological events compared to boys, higher α might be interpreted as reflecting a faster maturation in girls than in boys. In older age groups higher β power in girls has been found before (Matoušek and Petersén, 1973; Matsuura et al., 1985). We do not know why girls have higher β power than boys. A possible explanation might be that girls were less relaxed, and more alert during the experimental sessions, which would yield more fast and

fewer slow waves. However, no sex differences were found in slow waves (i.e. δ, θ and α bands).

Only a few studies thus far have been conducted on genetic and environmental influences on EEG parameters in children. For slightly older twins, ranging from 9 to 22 years of age, Dumermuth (1968) found that 6 MZ pairs showed larger resemblance than 4 DZ twin pairs. We know of only one other study that has estimated genetic and environmental influences on power of frequency bands in the EEG of a group of 5 year old children (Gavrish and Malykh, 1994). In agreement with our results, their abstract indicated high heritabilities for the 7.5–13 Hz frequency band which was in bins of 1.5 Hz. Other studies using large age ranges but including some 5 year olds (Vogel, 1958; Whitton et al., 1985) also agree with our results, in that high heritability was found for α power. The overall conclusion, therefore, must be that the individual differences in absolute and relative EEG power spectra seen at age 5 are largely genetically determined.

The heritabilities for absolute power of 5 year old children found in this study can be compared directly with heritabilities obtained in a sample of adolescent twin pairs, who participated in a similar study with an identical procedure, conducted at our laboratory (Van Beijsterveldt et al., 1996). Heritabilities tended to be a little bit higher in adolescence (mean heritability was about 90%, except for δ, for which heritability was about 75%). In both age cohorts it was shown that genetic factors explained the larger part of variance in EEG power spectra.

Estimating heritability by using the twin method can be confounded by a number of factors as indicated by Falconer (1989, pp. 174). Some of these factors, like the number of amnia and choria shared by MZ twins in utero, or parental treatment of the twins, will have an unpredictable effect. Other factors, like genotype-environment interaction, or the exact contemporaneity of twins as compared with singletons, would result in a larger estimate of environmental effects, and a lower estimate of genetic effects. Since heritabilities in this study are very high, these factors obviously are not very important.

Heritability estimates cannot be understood fully without a notion of the size of the measurement errors in obtaining the trait. In EEG measurements a good estimator of the measurement error is the use of split-half reliability. When MZ twins are compared with their cotwins, they can never be more alike than the split-half reliability of the trait. Therefore, split-half reliability of the trait gives an upper boundary for heritability. By the same token, a high correlation in MZ twins indicates that the split-half reliability of the trait under study must be high (Lykken, 1982). We calculated split-half reliabilities for absolute and relative power in 6 broadbands. All split-half correlations were very high, suggesting that only a very small part of the environmental variance is due to measurement error. Apart from measurement error, specific conditions of the experiment, time-of-day, duration of signal conditioning, mood state, temperature, etc. may create additional unique environmental variance that detracts from heritability. Such influences might be estimated by looking at temporal stability of the EEG parameters. Gasser et al. (1985) measured EEG power spectra twice in 10–13 year old children with a 10 months interval. The retest reliabilities of absolute power in δ, θ, $\alpha 1$, $\alpha 2$, $\beta 1$ and $\beta 2$ power were 0.59, 0.70, 0.80, 0.72, 0.58 and 0.66, respectively. Unfortunately, it is unclear to what extent the imperfect test-retest correlation is confounded by maturational effects. Measurements in Gasser's study were 10 months apart. In fact, the heritabilities found in our study (i.e. 55, 81, 81, 78, 73 and 64%, respectively), compare favorably with their test-retest correlations.

The large environmental influences for absolute power in the δ band on all frontal (Fp1, Fp2, F7, F3, F4, F8) leads may have resulted from true environmental influences, for instance related to drowsiness. Although children who were visibly drowsy were always removed from the analyses, at this age, drowsiness is not easily detected in the EEG, so it may have confounded our assessment of the causes of individual differences in δ. On the other hand, it is unclear why this did not affect h^2 in the θ band. An alternative explanation for the large environmental contribution to δ may be found in eye-movements. Because eye-movement are in the δ frequency range and because the frontal leads are most sensitive to admixture of EEG with EOG, it is tempting to suggest that the low h^2 in δ activity resulted from measurement error. In fact, the slight negative occipital-frontal gradient in h^2 in the other bands may also be related to admixture of the EEG with EOG. Finally, it was pointed out by Dumermuth and Molinari (1987) that EEG power may be decomposed into white, pink (amorphous or arrhythmic EEG) and colored ('true' EEG peak powers) components. The power in the δ bands is particularly affected by pink noise. Heritability may thus suffer from the influences of pink noise, instead of reflecting genetics of true δ activity.

Several authors have suggested that the developmental changes in the EEG power spectra can be seen as an index of CNS maturation (Matoušek and Petersén, 1973; Gasser et al., 1988). This age-EEG relationship is not necessarily linear and shows different patterns with topography such that posterior regions are seen to mature earlier than anterior ones (Matoušek and Petersén, 1973; Katada et al., 1981; Gasser et al., 1988). Our results could be interpreted as pointing to a strong genetic determination of CNS maturation around the 5th year of life. Also, since for both sexes the same genetic factors underlie power, maturation of the CNS seems controlled by the same set of genes in boys and girls.

If the development of rhythmical activity in the brain is strongly under genetic control, as we have shown in our study, one could be tempted to suggest that the development in cognitive functioning is under genetic control too.

In a series of articles Thatcher and coworkers have suggested that developmental changes in the EEG may closely reflect the stages proposed by Jean Piaget (Thatcher, 1991, 1992). The finding of high heritabilities for power in the current study appears to lend support to their idea that 'human cognitive development occurs ontogenetically, i.e. by the genetically programmed unfolding of specific brain functions and specific brain connections' (Thatcher et al., 1987). Clear links between EEG power and individual differences in cognitive ability have been suggested (Weiss, 1992), but remain to be established, both in adults and in children. It should be noted that the heritability of another electrophysiological index for cognitive functioning, the event related potential (ERP), does not show the same strong heritability as seen for background EEG. The twins measured in our study also participated in an ERP study, in which P300 was measured in an oddball task. Using a model that distinguished measurement error from true variance, heritabilities for real P300 amplitudes and latencies were still much lower (Van Baal et al., 1996). For Pz electrode position, h^2 at age 5 was 14% for target amplitude and 86% for non target amplitude, and 66% for both target and non target latencies. However, genetic effects are not fixed for life. We have shown high heritabilities in this age cohort, but other genetic factors might influence EEG power at a later age, depending, for example, on whether growth spurts take place, or whether more continuous growth of the brain is dominant in that period. Consequently, it might well be that the relative influences of genes and environment on electrophysiological indices change with age. Therefore, longitudinal twin data are needed to test the change in genetic contribution over time. The present data represent the starting point of such a longitudinal study.

Acknowledgements

The authors would like to thank R. Nieuwboer for software development, J. de Vries and R. Sijmons for technical support, and S. Kramer and C. Woudstra for assistance in data collection. The research reported here was supported by a grant from the Netherlands Organization for Scientific Research (NWO 575-65-052).

Appendix A. Twin correlations for log transformed absolute power and logit transformed relative power for 5 groups in 6 bands, 14 electrode positions

	Fp1	Fp2	F7	F3	F4	F8	C3	C4	T5	P3	P4	T6	O1	O2
δ: absolute power														
MZM	0.21	0.36	0.23	0.48	0.68	0.41	0.67	0.69	0.61	0.69	0.71	0.80	0.65	0.79
DZM	-0.21	0.01	0.05	0.48	0.47	0.22	0.59	0.51	0.50	0.45	0.35	0.31	0.34	0.41
MZF	0.42	0.39	0.70	0.38	0.57	0.64	0.50	0.47	0.32	0.52	0.56	0.65	0.63	0.58
DZF	0.01	0.04	-0.01	0.15	0.05	0.10	-0.12	0.07	-0.04	-0.04	0.07	0.04	0.09	0.19
DOS	0.22	0.21	0.43	0.28	0.19	0.24	0.34	0.52	0.25	0.58	0.66	0.63	0.55	0.62
θ: absolute power														
MZM	0.59	0.75	0.60	0.76	0.85	0.67	0.84	0.83	0.84	0.89	0.88	0.80	0.87	0.85
DZM	0.32	0.44	0.63	0.47	0.49	0.53	0.48	0.39	0.53	0.48	0.43	0.43	0.54	0.53
MZF	0.71	0.78	0.73	0.71	0.78	0.73	0.82	0.80	0.80	0.84	0.85	0.83	0.86	0.83
DZF	0.47	0.46	0.42	0.49	0.47	0.38	0.33	0.37	0.26	0.29	0.32	0.27	0.24	0.28
DOS	0.36	0.28	0.45	0.33	0.35	0.43	0.45	0.52	0.38	0.52	0.51	0.44	0.55	0.47
α1: absolute power														
MZM	0.49	0.70	0.66	0.71	0.81	0.73	0.86	0.84	0.83	0.86	0.86	0.80	0.87	0.89
DZM	0.36	0.44	0.50	0.55	0.53	0.43	0.63	0.57	0.64	0.63	0.56	0.64	0.69	0.67
MZF	0.84	0.90	0.79	0.81	0.88	0.86	0.86	0.89	0.91	0.89	0.90	0.91	0.90	0.92
DZF	0.66	0.54	0.55	0.59	0.55	0.36	0.57	0.50	0.44	0.50	0.50	0.53	0.47	0.54
DOS	0.24	0.22	0.25	0.20	0.31	0.39	0.46	0.42	0.23	0.43	0.41	0.31	0.38	0.35
α2: absolute power														
MZM	0.52	0.83	0.62	0.69	0.82	0.69	0.89	0.89	0.86	0.90	0.87	0.84	0.80	0.84
DZM	0.17	0.40	0.39	0.56	0.54	0.14	0.45	0.48	0.55	0.59	0.53	0.55	0.63	0.70
MZF	0.79	0.81	0.67	0.75	0.82	0.80	0.77	0.77	0.83	0.88	0.88	0.87	0.83	0.83
DZF	0.46	0.42	0.32	0.46	0.53	0.31	0.43	0.46	0.29	0.40	0.48	0.46	0.44	0.52
DOS	0.17	0.09	0.26	0.23	0.30	0.27	0.35	0.47	0.40	0.44	0.35	0.41	0.53	0.53
β1: absolute power														
MZM	0.52	0.72	0.64	0.76	0.76	0.59	0.85	0.86	0.78	0.88	0.87	0.76	0.71	0.76
DZM	0.04	0.58	0.37	0.60	0.64	0.29	0.55	0.53	0.40	0.52	0.38	0.38	0.58	0.56
MZF	0.60	0.59	0.55	0.55	0.73	0.74	0.77	0.86	0.65	0.85	0.87	0.81	0.83	0.79
DZF	0.15	0.05	0.16	0.32	0.41	0.32	0.29	0.28	0.31	0.34	0.33	0.23	0.35	0.36
DOS	0.05	0.08	0.21	0.14	0.19	0.22	0.24	0.28	0.16	0.27	0.30	0.35	0.46	0.43

	Fp1	Fp2	F7	F3	F4	F8	C3	C4	T5	P3	P4	T6	O1	O2
β2: absolute power														
MZM	0.44	0.58	0.55	0.79	0.75	0.52	0.82	0.85	0.58	0.82	0.82	0.76	0.74	0.75
DZM	0.14	0.34	0.30	0.61	0.62	0.35	0.48	0.64	0.28	0.51	0.45	0.37	0.62	0.65
MZF	0.45	0.27	0.52	0.55	0.69	0.62	0.69	0.77	0.43	0.67	0.76	0.68	0.69	0.72
DZF	-0.04	-0.16	0.17	0.37	0.41	0.23	0.37	0.35	0.24	0.32	0.38	0.32	0.33	0.43
DOS	0.27	0.41	0.45	0.45	0.40	0.22	0.56	0.56	0.09	0.47	0.54	0.56	0.53	0.48
δ: relative power														
MZM	0.51	0.43	0.54	0.66	0.75	0.61	0.75	0.71	0.71	0.86	0.74	0.68	0.81	0.83
DZM	0.29	0.16	0.18	0.32	0.14	0.23	0.11	0.01	0.17	0.02	0.25	0.12	0.34	0.34
MZF	0.45	0.29	0.78	0.68	0.63	0.64	0.71	0.66	0.81	0.77	0.68	0.57	0.72	0.66
DZF	0.12	0.17	0.20	-0.11	0.03	0.11	0.03	0.17	0.00	0.14	0.16	0.18	0.05	0.18
DOS	0.35	0.43	0.10	0.25	0.20	0.08	0.31	0.36	0.48	0.45	0.33	0.37	0.26	0.21
θ: relative power														
MZM	0.63	0.62	0.72	0.77	0.84	0.76	0.80	0.82	0.79	0.86	0.88	0.77	0.89	0.88
DZM	0.39	0.35	0.27	0.21	0.25	0.34	0.18	0.13	0.30	0.11	0.40	0.33	0.43	0.47
MZF	0.59	0.42	0.83	0.76	0.69	0.71	0.80	0.82	0.81	0.84	0.80	0.75	0.79	0.76
DZF	0.20	0.14	0.47	0.32	0.37	0.23	0.42	0.42	0.38	0.48	0.49	0.56	0.38	0.45
DOS	0.42	0.52	0.23	0.40	0.41	0.30	0.46	0.63	0.45	0.47	0.48	0.36	0.38	0.42
α1: relative power														
MZM	0.62	0.48	0.48	0.74	0.74	0.52	0.74	0.74	0.85	0.83	0.77	0.78	0.88	0.90
DZM	0.18	0.13	0.39	0.46	0.46	0.59	0.53	0.54	0.39	0.50	0.49	0.40	0.45	0.53
MZF	0.63	0.56	0.80	0.76	0.78	0.79	0.79	0.71	0.78	0.75	0.72	0.81	0.76	0.79
DZF	0.43	0.44	0.37	0.43	0.49	0.42	0.47	0.52	0.50	0.57	0.52	0.58	0.51	0.48
DOS	0.36	0.50	0.18	0.31	0.33	0.11	0.49	0.51	0.20	0.37	0.36	0.22	0.13	0.26
α2: relative power														
MZM	0.27	0.29	0.25	0.70	0.82	0.55	0.83	0.89	0.88	0.89	0.89	0.85	0.87	0.82
DZM	-0.05	-0.03	0.23	0.35	0.20	0.10	0.32	0.39	0.56	0.45	0.36	0.48	0.43	0.49
MZF	0.48	0.45	0.77	0.79	0.81	0.74	0.74	0.64	0.76	0.79	0.75	0.72	0.67	0.56
DZF	0.40	0.45	0.31	0.45	0.54	0.55	0.43	0.57	0.47	0.53	0.53	0.42	0.49	0.43
DOS	0.33	0.36	0.18	0.09	0.18	-0.01	0.21	0.41	0.44	0.50	0.50	0.44	0.56	0.63
β1: relative power														
MZM	0.19	0.24	0.26	0.68	0.72	0.40	0.72	0.74	0.72	0.83	0.86	0.68	0.77	0.82
DZM	-0.16	-0.03	0.18	0.26	0.14	0.02	0.25	0.19	0.16	0.26	0.27	0.20	0.34	0.43
MZF	0.41	0.40	0.73	0.81	0.79	0.70	0.88	0.81	0.72	0.82	0.87	0.83	0.81	0.79
DZF	0.24	0.41	0.24	0.37	0.39	0.42	0.35	0.33	0.40	0.46	0.48	0.43	0.44	0.48
DOS	0.41	0.30	0.26	0.36	0.39	0.24	0.34	0.35	0.36	0.43	0.42	0.48	0.50	0.27
β2: relative power														
MZM	0.13	0.33	0.42	0.74	0.80	0.43	0.74	0.75	0.66	0.80	0.79	0.61	0.80	0.82
DZM	0.00	0.01	0.25	0.32	0.22	0.27	0.28	0.35	0.25	0.29	0.33	0.22	0.44	0.31
MZF	0.38	0.24	0.60	0.78	0.75	0.48	0.80	0.73	0.58	0.70	0.83	0.76	0.78	0.82
DZF	0.09	0.16	0.28	0.44	0.36	0.18	0.42	0.34	0.41	0.43	0.40	0.43	0.26	0.40
DOS	0.48	0.40	0.30	0.40	0.41	0.17	0.36	0.37	0.20	0.42	0.44	0.30	0.32	0.29

References

Benninger, C., Matthis, P. and Scheffner, D. EEG development of healthy boys and girls: results of a longitudinal study. Electroenceph. clin. Neurophysiol., 1984, 57: 1–12.

Blinkov, S.M. and Glezer, I.I. The Human Brain in Figures and Tables: a Quantitative Handbook. Plenum, New York, 1968.

Boomsma, D.I. Current status and future prospects in twin studies of the development of cognitive abilities: infancy to old age. In: T.J. Bouchard Jr. and P. Propping (Eds.), Twins as a Tool of Behavioral Genetics. Wiley, Chichester, 1993, pp. 67–82.

Boomsma, D.I. and Gabrielli, Jr., W.F. Behavioral genetic approaches to psychophysiological data. Psychophysiology, 1985, 22: 249–260.

Boomsma, D.I., Orlebeke, J.F. and Van Baal, G.C.M. The Dutch twin register: growth data on weight and height. Behav. Genet., 1992, 22: 247–251.

Brillinger, D.R. Time Series: Data Analyses and Theory. Holt, Rinehart and Winston, London, 1975.

Chavance, M. and Samson-Dollfus, D. Analyse spectrale de l'EEG de l'enfant normal entre 6 et 16 ans: choix et validation des parametres les plus informationnels. Electroenceph. clin. Neurophysiol., 1978, 45: 767–776.

Chugani, H.T., Phelps, M.E. and Mazziotta, J.C. Positron emission tomography study of human brain functional development. Ann. Neurol., 1987, 22: 487–497.

Courchesne, E. Chronology of postnatal human brain development: event-related potential, positron emission tomography, myelinogenesis, and synaptogenesis studies. In: J. Rohrbaugh, R. Parasuraman and R. Johnson (Eds.), Event Related Brain Potentials: Basic

Issues and Applications. Oxford University Press, New York, 1990, pp. 210–241.

Dumermuth, G. Variance spectra of electroencephalograms in twins: a contribution to the problem of quantification of EEG background activity in childhood. In: P. Kellaway and I. Petersén (Eds.), Clinical Electroencephalography of Children. Almqvist and Wiksell, Stockholm, 1968, pp. 119–154.

Dumermuth, G. and Molinari, L. Spectral analysis of the EEG: some fundamentals revisited and some open problems. Neuropsychobiology, 1987, 17: 85–99.

Falconer, D.S. Introduction to Quantitative Genetics, 3rd edn. Longman, Essex, 1989.

Gasser, T., Bächer, P. and Steinberg, H. Test-retest reliability of spectral parameters of the EEG. Electroenceph. clin. Neurophysiol., 1985, 60: 312–319.

Gasser, T., Verleger, R., Bächer, P. and Sroka, L. Development of the EEG of school-age children and adolescents, I: analysis of band power. Electroenceph. clin. Neurophysiol., 1988, 69: 91–99.

Gavrish, N. and Malykh S.B. The nature of the variability in the individual differences of the frequency characteristics of the α-rhythm EEG in 6- to 8-year-old children (abstract, Russian). Zh. Vyss. Nervn. Deyat. im. I. P. Pavlova, 1994, 44: 8–17.

Goldman-Rakic, P.S. Development of cortical circuitry and cognitive function. Child Dev., 1987, 58: 601–622.

Goldsmith, H.H. A zygosity questionnaire for young twins: a research note. Behav. Genet., 1991, 21: 257–269.

Hudspeth, W.J. and Pribram, K.H. Psychophysiological indices of cerebral maturation. Int. J. Psychophysiol., 1992, 12: 19–29.

Huttenlocher, P. Synaptic density in human frontal cortex: developmental changes and effects of aging. Brain Res., 1979, 163: 195–205.

Jasper, H. Report of the committee on methods of clinical examination in electroencephalography. Electroenceph. clin. Neurophysiol., 1958, 10: 370–375.

John, E. The role of quantitative EEG topographic mapping or 'neurometrics' in the diagnosis of psychiatric and neurological disorders: the pros. Electroenceph. clin. Neurophysiol., 1989, 73: 2–4.

John, E., Ahn, H. and Prichep, L. Developmental equations for the electroencephalogram. Science, 1980, 210: 1255–1258.

Katada, A., Ozaki, H., Suzuki, H. and Suhara, K. Developmental characteristics of normal and mentally retarded children's EEGs. Electroenceph. clin. Neurophysiol., 1981, 52: 192–201.

Lykken, D. Research with twins: the concept of emergenesis (presidential address, 1981). Psychophysiology, 1982, 19: 361–373.

Matoušek, M. and Petersén, I. Frequency analysis of the EEG in normal children and adolescents. In: P. Kellaway and I. Petersén (Eds.), Automation of Clinical Electroencephalography. Raven Press, New York, 1973, pp. 75–102.

Matsuura, M., Yakamoto, K., Fukuzawa, H., Okubo, Y., Uesugi, H., Moriiwa, M., Kojima, T. and Shimazono, Y. Age development and sex differences of various EEG elements in healthy children and adults: quantification by a computerized wave form recognition method. Electroenceph. clin. Neurophysiol., 1985, 60: 394–406.

Matthis, P., Scheffner, D., Benninger, C., Lipinski, C. and Stolzis, L. Changes in the background activity of the electroecephalogram according to age. Electroenceph. clin. Neurophysiol., 1980, 49: 626–635.

Neale, M.C. Mx: Statistical Modeling, 2nd edn. Department of Psychiatry, Box 710 MCV, Richmond, VA 23298, 1994.

Neale, M.C. and Cardon, L.R. Methodology for Genetic Studies of Twins and Families. NATO ASI series: behavioral and social sciences. Kluwer Academic, Dordrecht, 1992.

Niedermeyer, E. and Lopes da Silva, F. Electroencephalograpy, Basic Principles, Clinical Applications and Related Fields, 3rd edn. Williams and Wilkins, Baltimore, 1993.

Nowakowski, R. Basic concepts of CNS development. Child Dev., 1987, 58: 568–595.

Petersén, I. and Eeg-Olofsson, O. The development of the electroencephalogram in normal children from the age of 1 through 15 years: non-paroxysmal activity. Neuropäediatrie, 1971, 2: 247–304.

Pivik, R., Broughton, R., Coppola, R., Davidson, R., Fox, N. and Nuwer, M. Guidelines for the recording and quantitative analysis of electroencephalographic activity in research contexts. Psychophysiology, 1993, 30: 547–558.

Plomin, R., DeFries, J. and McClearn, G. Behavioral Genetics: a Primer. Freeman, San Francisco, 1990.

Samson-Dollfus, D. and Goldberg, P. Electroencephalographic quantification by time domain analysis in normal 7–15 year old children. Electroenceph. clin. Neurophysiol., 1979, 46: 147–154.

Sutcliffe, J. and Milner, R. Brain specific gene expression. Trends Biochem. Sci., 1984, 9: 95–99.

Thatcher, R.W., Walker, R.A. and Guidice, S. Human cerebral hemispheres develop at different rates and ages. Science, 1987, 236: 1110–1113.

Thatcher, R.W. Maturation of the human frontal lobes: physiological evidence for staging. Dev. Neuropsychol., 1991, 7: 397–419.

Thatcher, R.W. Cyclic cortical reorganization during early childhood. Brain Cogn., 1992, 20: 24–50.

Thatcher, R.W. Cyclic cortical reorganization, origins of human cognitive development. In: G. Dawson and K.W. Fischer (Eds.), Human Behavior and the Developing Brain. Guildford Press, New York, 1994, pp. 232–266.

Van Baal, G.C.M., De Geus, E.J.C. and Boomsma, D.I. Longitudinal study of genetic influences on ERP-P3 during childhood. Dev. Neuropsychol. (Behavioral Genetics), 1996, in press.

Van Beijsterveldt, C.E.M. and Boomsma, D.I. Genetics of the human electroencephalogram (EEG) and event-related brain potentials (ERPs): a review. Hum. Genet, 1994, 94: 319–330.

Van Beijsterveldt, C.E.M., Molenaar, P.C.M., De Geus, E.J.C. and Boomsma, D.I. Heritability of human brain functioning as assessed by electroencephalography (EEG). Am. J. Hum. Genet., 1996, 58: 562–573.

Vogel, F. Über die erblichkeit des normalen elektroenzephalogramms. Vergleichende untersuchungen an ein- und zweieiigen zwillingen. Georg thieme verlag, Stuttgart, 1958.

Weiss, V. The relationship between short-term memory capacity and EEG power spectral density. Biol. Cybern., 1992, 68: 165–172.

Whitton, J.L., Elgie, S.M., Kugel Herb, and Moldofsky, H. Genetic dependence of the electroencephalogram bispectrum. Electroenceph. clin. Neurophysiol., 1985, 60: 293–298.

Yakovlev, P.I. and Lecours, A. The myelogenetic cycles of regional maturation of the brain. In: A. Minkovski (Ed.), Regional Development of the Brain in Early Life. Blackwell, Oxford, 1967, pp. 3–70.