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Heritability of Human Brain Functioning as Assessed by Electroencephalography

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Summary

To study the genetic and environmental contributions to individual differences in CNS functioning, the electroencephalogram (EEG) was measured in 213 twin pairs age 16 years. EEG was measured in 91 MZ and 122 DZ twins. To quantify sex differences in the genetic architecture, EEG was measured in female and male same-sex twins and in opposite-sex twins. EEG was recorded on 14 scalp positions during quiet resting with eyes closed. Spectral powers were calculated for four frequency bands: delta, theta, alpha, and beta. Twin correlations pointed toward high genetic influences for all these powers and scalp locations. Model fitting confirmed these findings; the largest part of the variance of the EEG is explained by additive genetic factors. The averaged heritabilities for the delta, theta, alpha, and beta frequencies was 76%, 89%, 89%, and 86%, respectively. Multivariate analyses suggested that the same genes for EEG alpha rhythm were expressed in different brain areas in the left and right hemisphere. This study shows that brain functioning, as indexed by rhythmic brain-electrical activity, is one of the most heritable characteristics in humans.

Introduction

The study of possible genetic influences on normal and abnormal behavior in humans has received much attention. In the age of molecular biology the chance to unravel the genetic basis of human behavior is enlarged, as, for example, in the localization of the gene for Huntington disease. Human behavior is a complex phenotype to study, because behavior is in continuous interaction with the environment. This makes the search for genetic variability in human behavior sometimes difficult. Genetic influences on behavior are most likely to be expressed via the brain. By studying human brain function it may be possible to find genetically determined influences on behavior. Little is known about genetic influences on individual differences in the functioning of the CNS.

To examine the influence of genetic factors on individual differences in CNS functioning, neurophysiological methods such as electroencephalogram (EEG) recordings can be used. The EEG is a registration of the ongoing rhythmical electrical activity of the brain over a short period of time and provides a direct measure of the present functional state of the brain and of its different levels of arousal. EEG is due mostly to the synchronous activity of pyramidal neurons in the cortex (Nunez 1981). The mechanism of the generation of EEG rhythms is largely unknown. Presumably, thalamocortical and corticocortical systems play a role in the generation of, for example, the alpha rhythm (Steriade et al. 1990).

The EEG can be described by various parameters, such as amplitude and rhythm. Often the EEG is analyzed in forms of power (in Hz) per frequency band, by use of Fourier analysis on short time series. In a normal waking adult human, two rhythms dominate in the resting EEG. A posterior rhythmic activity in the frequency range of 8–13 Hz (alpha), generally with higher voltage over the occipital areas, is observed when subjects close their eyes under the conditions of physical relaxation and relative mental inactivity. A faster rhythm (13–20 Hz), with a lower voltage and an irregular pattern distributed diffusely over the scalp, appears in alert subjects.

Although the EEG is a complex trait that varies in many dimensions, such as distribution of frequencies, amplitudes over the different brain areas, and morphology of waveforms, it tends to be a stable individual characteristic. Test-retest correlation coefficients for EEG power were ~.8 for both absolute and relative power, with a 12–16-wk interval between the measurements (Stassen et al. 1987; Pollock et al. 1991; Salinsky et al. 1991). Even for longer intervals (with an average 10-mo interval), the test-retest reliability stays ~.7 (Gasser et al. 1985). Among individuals the EEG varies considerably. Simonava and Roth (1967) found alpha amplitudes of 20–60 μV in 66% of their subjects; values <20 μV were found in 28% of the sample, and values

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>60 μV were found in 6% of the sample. The stability in a single individual over time, combined with marked interindividual variability, poses the question of the genetic determination of brain activity.

Several twin and family studies have investigated the role of genetic factors in individual differences in EEG parameters. Since the earliest twin studies, it has been clear that the human EEG is mainly determined by genetic factors. Under visual inspection, a high degree of similarity in EEG parameters was found for MZ twins (Davis and Davis 1936; Raney 1939; Lennox et al. 1945). These observations were confirmed by more advanced recording methods. For various EEG parameters, high similarities were found for MZ twins, and moderate similarities were found for DZ twins (for a review, see van Beijsterveldt and Boomsma 1994). The normal EEG rhythm appears to be influenced by many genes (Vogel 1970). Recently, for the low-voltage EEG, a rare variant of a the normal human EEG, localization of a gene has been reported (Anokhin et al. 1992; Steinlein et al. 1992).

Part of the variability in EEG is induced by age. During the maturation of the brain, leading to functional differentiation of various brain areas, the EEG generally decreases in amplitude, and slow activity is substituted by fast activity (Matoušek and Petersén 1973). Maturation of the brain probably extends into adulthood (Fisher and Rose 1994). Among individuals, large differences exist in the rate of development. Vogel (1958), who investigated different EEG parameters in a large group of twins age 6–80 years, found considerable interindividual differences in EEG maturation, but for MZ twins a complete concordance of EEG was found, which probably indicates that the speed of maturation is genetically determined. It is unclear whether the genetic contribution to EEG parameters is stable over different ages. Most studies consist of small samples of family members and have pooled data from different age groups.

During certain developmental periods the genetic contribution may differ for slow and fast EEG frequencies or for different brain areas. Maturation of the brain is not only a continuous growth process, but discrete growth spurts appear in specific anatomical locations at specific periods (Thatcher 1992). Advances in the technology underlying the recording and analysis of EEG activity make it possible to study a range of EEG frequencies over different brain areas.

Beside more sophisticated EEG technology, the development of multivariate techniques in genetic model fitting (Martin and Eaves 1977; Boomsma and Molenaar 1986) allows more insight to be gained into genetic processes underlying the EEG recorded for different brain areas. It seems that in the prefrontal cortex corticocortical interconnections are more extensive and appear to be organized in a way fundamentally different from those in the posterior cortex (Gevins and Illes 1991). With multivariate analyses the genetic and environmental bases of covariance between different brain areas may be studied, and questions regarding the involvement of different gene systems may be addressed.

Most twin and family studies that have investigated genetic influences on EEG parameters have used only a few subjects in a large age range. None of the studies has quantified the genetic contribution as a function of sex. Because age and sex are important determinants of EEG parameters, EEG in the present study was measured in a small age range (mean age = 16 years; SD = 0.55 years) and in female, male, same-sex, and opposite-sex twin pairs. The EEG was measured at 14 electrode positions during rest, in 91 MZ and 122 DZ twins.

We investigated the genetic influences on different rhythms of the EEG in different brain areas and addressed the questions of whether (1) heritability is different for the four main rhythmic EEG frequencies, i.e., delta, theta, alpha, and beta; (2) the same genes contribute to EEG variability in the left and right hemisphere; (3) the heritability is the same in males and females and whether the same genes are expressed in males and females; and (4) the heritability of delta, theta, alpha, and beta is the same for various brain areas (frontal, central, parietal, occipital, and temporal) and whether the same genes are expressed in these areas of the brain.

Subjects and Methods

Subjects

A group of 213 adolescents twins (mean age = 16.18 years; SD = 0.55 years) participated in the study. Addresses of twin pairs were obtained from participants in a large questionnaire study on health-related behaviors (Boomsma et al. 1994). Subjects were asked by letter to participate.

The subjects were divided into five groups, by sex and zygosity: 39 MZ males (MZM), 36 DZ males (DZM), 52 MZ females (MZF), 38 DZ females (DZF), and 48 twins of opposite sex (DOS). For 114 same-sex twins, zygosity was determined by blood and DNA typing. For the other same-sex twins, zygosity was determined by a questionnaire, completed by the mother of the twins and consisting of items about physical similarity (similarity of face, eye color, hair color, and skin color) and the frequency of confusion of the twins by family and strangers. Seventeen twin pairs completed the questionnaires themselves. Agreement between zygosity based on this questionnaire and zygosity based on blood group polymorphism and DNA fingerprinting was 95%.

Six subjects were discarded from further analyses because of recording artifacts in one or more EEG channels. This left 37 MZM, 35 DZM, 52 MZF, 37 DZF, and 46 DOS pairs for analysis.

Procedure

The measurement session lasted 3 ½ h and took place in the morning or in the afternoon. Each subject visited

the laboratory on the same day and was tested during the same segment of the day as was his or her co-twin. The session consisted of four tests: measurement of the EEG/ERP, measurement of nerve conduction velocity (Rijsdijk et al. 1995), reaction time, and intelligence tests. After arrival, a short explanation of the experiment was given, for familiarization with the procedure. One twin started with the EEG measurement, and the other one started with measurement of the other variables. After the EEG and EOG electrodes were put on, the subjects lay down on a bed in an electrically shielded and soundproof cabin. After the EEG and EOG signals were controlled, instructions were displayed on a black-and-white monitor attached to the ceiling. EEG was recorded during three experimental conditions, in fixed order: during an auditive-habituation task, during a visual oddball task, and in a rest condition. In this paper the results of the EEG in the rest condition are presented.

In the rest condition, EEG was recorded during a period of 3 min, in which the subject closed the eyes. In this condition the alpha rhythm is clearly visible. If artifacts occurred during the recording, the recording period was lengthened to 4 min.

EEG Recording

Tin electrodes mounted in an electrocap were used for measuring EEG activity. Scalp locations were prefrontal (Fp1 and Fp2), midfrontal (F3 and F4), lateral frontal (F7 and F8), central (C3 and C4), parietal (P3 and P4), occipital (O1 and O2), and temporal (T5 and T6), according the 10–20 system (Jasper 1958). Linked earlobes were used as references, according the method described by Pivik et al. (1993). In brief, two separate preamplifiers with high-input impedance for each of the reference electrodes were used, and the output was linked electrically. With the ears linked this way, the effects of possible imbalances in electrode impedance are prevented.

The electrode impedance for EEG and EOG was <5 kΩ. Tin electrodes were placed at the canthus of each eye, for recording horizontal movements. For vertical movement, EOG was recorded from intraorbital and supraorbital electrodes, in line with the pupil of the left eye. A ground electrode was attached to the prefrontal midposition (Fpz). For both EEG and EOG, ECI (electrogel) EEG paste was used.

All EEG signals and EOG signals were displayed and recorded by a 18-channel Nihon Kohden electroencephalograph (type EEG-4414A1K). For EEG and EOG recordings, the time constant was 5 s, and a low-pass frequency with a 35-Hz cutoff frequency was used. Subsequently, signals were sent to a 12-bit analog-digital converter and were computer-stored for off-line processing. During the EEG recording, the sampling rate of the AD converter was set to 250 Hz. A set of 100-μV sine waves was used for calibration for each of the 16 electrodes prior and after recording.

Data Processing

Preprocessing of the EEG consisted of dividing the EEG signal into epochs of 2 s. After automatic removal of epochs with artifacts (e.g., clipping), Fast Fourier Transformation (FFT) was applied to the 2-s epochs. A minimum of 30 epochs were required for further analyses. Subsequently, eye movements were removed by means of a dynamic regression routine in the frequency domain (Brillinger 1975). The direct-current offset was removed from the data by calculating the mean of the epoch and subtracting it from each point. Smoothed powers for frequency in the range of 0.5–30 Hz, with 0.5-Hz steps, were calculated by averaging the power values over the valid epochs. The resulting power values were summed together into broad bands: delta (1.5–3.5 Hz), theta (4–7.5 Hz), alpha (8–12.5 Hz), and beta (13–25 Hz). Total power was the sum of the absolute powers in these bands. To transform the powers to a Gaussian distribution, the EEG power bands (absolute powers) were log-transformed with $\log 10(x)$ (Pivik et al. 1993). The percentage of variance explained by each band, the relative power, was calculated by dividing the separate bands by the total power.

Statistical Analysis

To test whether there were any mean differences between males and females or between MZ and DZ twins, MANOVA (SPSS) was used. The EEG power bands were used as the dependent variables, with scalp locations (Fp1/Fp2, F3/F4, F7/F8, C3/C4, P3/P4, O1/O2, and T5/T6), hemisphere (left and right), and birth order (first and second born) as within-pair factors and with sex and zygosity as between-pair factors. Sex and zygosity effects were tested in MZM and DZM and in the MZF and DZF, only.

Univariate Genetic Analyses

For each electrode position and for each power (delta, theta, alpha, and beta), correlations were computed for MZM, DZM, MZF, DZF, and DOS twin pairs. The relative contributions of genetic influences to individual differences in EEG parameters were estimated by the method of genetic model fitting (Eaves et al. 1978; Boomsma and Gabrielli 1985; Neale and Cardon 1992).

In genetic model fitting the variation in the observed phenotype is decomposed into genetic and environmental variance. The genetic variance may be due to additive (A) or dominance (D) genetic influences, and the environmental variance may be due to environmental factors shared by twins reared in the same family (C) and to the nonshared environmental factors (E). Their influence on the phenotype is given by parameters a, d, c, and e, which are equivalent to the standardized regression coefficients of the phenotype on A, D, C, and E, respectively. The amount of variance due to each source is the square of these parameters.

To estimate parameters a, d, c, and e, for each power and for each electrode position, the data on twin 1 and twin 2 were summarized into 2 × 2 variance-covariance matrixes computed by Prelis (Jöreskog and Sörbom 1986). Mx (Neale 1994) was used to fit univariate models separately for each power and each electrode position, by the method of maximum likelihood. The overall goodness of fit of a model was assessed by the χ^2 goodness-of-fit statistic (Heath et al. 1989; Neale and Cardon 1992). A large χ^2 indicates a poor fit, whereas a small χ^2 indicates that the data are consistent with the model. The significance of the latent factors D (or C) and A were tested by likelihood-ratio tests by comparing the full genetic model to submodels. A significantly worse fit than the full model indicates the significance of the latent factor.

Sex differences in genetic architecture can result from differences in magnitude of the genetic effects and/or the environmental experiences. Another possibility is that different genes are expressed in the observed phenotype in males versus females. To test the first hypothesis, a model that equaled the genetic and environmental estimates for males and females was compared with a model that allowed for different estimates in males versus females. The second hypothesis was tested by estimating the genetic correlation between the DOS twins, instead of fixing it at .5.

Bi- and Multivariate Analysis

To test the hypothesis that the same genes influence the EEG in the left and right hemispheres, the contribution of genetic and environmental factors to the covariances of EEG powers obtained at left and right brain positions was estimated in bivariate analyses. The model is shown in figure 1, with a common genetic and a common environmental factor and with one specific genetic and one specific environmental factor. The two hypotheses to be tested were (1) whether one common genetic factor influences EEG in the left and right hemisphere or whether an additional, hemisphere-specific factor is needed and (2) that there is no environmental covariance between the two hemispheres. To test the first hypothesis, the specific genetic factor was constrained at zero. To test the second hypothesis, the common environmental factor was constrained at zero. These submodels were compared by hierarchical χ^2 tests.

Next, the genetic and environmental contributions to the covariances of the alpha power recorded at prefrontal, midfrontal, lateral frontal, central, temporal, parietal, and occipital areas, separately for the left and right hemispheres, were calculated, to assess to what extent the same genes were expressed in these brain areas. A triangular decomposition, which may be compared with principal component analysis, was used (Neale and Cardon 1992) to obtain estimates of the genetic and environmental correlations between the electrical activities of different brain areas.

Results

Means

In figure 2 an example is shown of a raw EEG signal, for an MZ twin pair and for a DZ twin pair. It shows both the similarity within an MZ twin pair and the interindividual variation. The power spectrum as a result of the fast Fourier transformation of the raw EEG signal of all twins is shown in figure 3. Highest power is found at the posterior brain areas (P3, P4, O1, and O2), with a peak around the 10-Hz frequency; in the anterior regions (Fp1, Fp2, F3, and F4) the power is much lower and peaks at lower frequencies. In figure 4 the absolute and relative powers for each EEG frequency band are given for each scalp location separately. The figure clearly shows the higher alpha power at posterior positions. At the anterior positions the lower frequencies bands, delta and theta, dominate.

For the statistical and genetic analysis, log-transformed values were used. None of the EEG frequency bands showed a significant difference, in power, between either the sexes or the zygosities. For all frequency bands the amplitude in the right hemisphere was significantly larger than that in the left hemisphere. The amplitude was larger for posterior scalp locations and became smaller in frontal scalp locations (all F ratios >100). The smallest amplitudes were found for scalp locations F7 and F8. The larger amplitude in the right hemisphere held for all scalp locations except the occipital locations, for which the amplitudes were equal (interaction effect of scalp location × hemisphere).

Univariate Genetic Analyses for the Different EEG Rhythms and Brain Areas

Appendix A shows the twin correlations for zygosity × sex groups, for all powers. These data indicate that genetic factors play an important role in EEG variability. For all EEG powers and scalp locations, the MZ correlations were large, ~.85, and the DZ correlations were approximately half of those for MZ. Appendix B presents the χ^2 for the best-fitting models. For most EEG rhythms and all brain areas, an AE model is the best-fitting model.

Delta.—The MZ correlations for the delta power were lower than those for the other EEG powers. Particularly for the frontal scalp locations, the MZF correlations were lower; over all scalp locations, the average MZF correlation was lower (.7) than the average MZM correlation (.8). The DZ correlations were approximately half of the MZ correlations. For electrode positions F3, F4, C3, P3, O1, and O2, the DZF correlations were almost equal to the MZF correlations, suggesting shared environment influences. However, the DOS correlation did not support such sex differences. If genetic factors contribute to the variance in males but not to that in females, then the DOS correlations should be

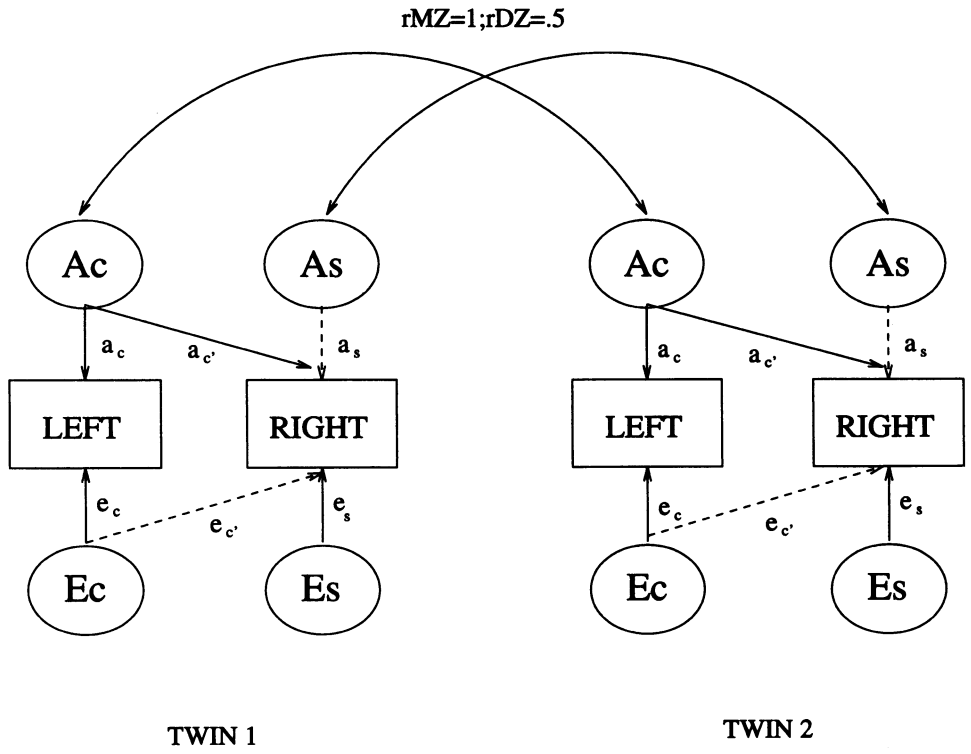

Figure 1 Bivariate genetic path model. "LEFT" and "RIGHT" denote the observed EEG power in left and right hemispheres in the youngest (twin 1) and oldest (twin 2) twins. "Ac" and "Ec" denote, respectively, the additive genetic and nonshared environmental factors common to the left and right hemispheres. "As" and "Es" are, respectively, specific additive genetic and specific nonshared environment unique for the right hemisphere. The dotted lines represent the paths that were constrained to be zero in the submodels.

zero. In addition, model-fitting results for these data do not suggest significant shared environment influences. Nevertheless, for scalp locations F4, F7, C3, P3, and P4, significant sex differences were found. For the remaining scalp locations, AE models without sex differences were the best-fitting models. In figure 5 the proportion of variance explained by additive genetic factors (h^2) is given. The heritabilities averaged over the frontal scalp locations were 70%; they were 80% for the posterior locations. For brain areas for which models with sex differences were found, the females heritabilities were somewhat lower.

Theta.—For theta, all MZ correlations were high. Averaged over all scalp locations, the MZ correlations were ~.9, both for males and for females. The averaged DZ correlations were half the averaged MZ correlations. AE models were the best-fitting models for most of the scalp locations, except for C4 and P3; for these locations, a model with sex differences was found. However, the heritabilities did not show large differences between males and females. Scalar models were found for scalp locations F4 and C3, meaning that the total amount of variance differed significantly between the sexes; but there were no sex differences, in genetic architecture, between males and females.

Alpha.—For alpha, both for females and for males, the MZ correlations were larger than the DZ correlations, over all scalp locations. AE models were the best-fitting models for all areas of the brain, without sex differences. The heritability, averaged over all scalp locations, was 89%.

Beta.—The MZM and MZF correlations for all scalp locations equaled the MZ correlations of alpha and theta. However, the DZF correlations were lower than expected on basis of genetic relatedness; this was emphasized in central and parietal scalp locations. The low DZF correlation could point to genetic effects that are due to dominance. With model fitting, genetic dominance was indicated for two scalp locations; for the other scalp locations the mode of the genetic inheritance was additive. With model fitting, no sex differences were found. For all scalp locations the variance explained by genetic factors was high.

Bi- and Multivariate Analysis for the EEG Rhythms and Brain Areas

In table 1 the results of the bivariate analyses are summarized. Tests for sex differences were performed only when differences existed in the univariate case. The models shown underlined in table 1 gave the best fit. The covariance between the electrode combinations of the left and right hemispheres seemed influenced primar-

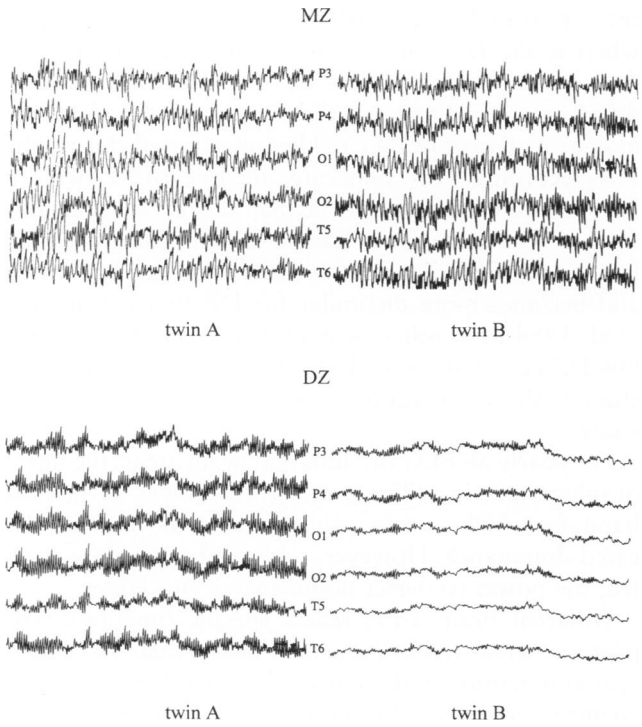

Figure 2 Example of a raw EEG signal for the youngest (twin A) and oldest (twin B) of an MZ (*upper panel*) and DZ (*lower panel*) twin pair. The EEG signals were recorded on left and right parietal, left and right occipital, and left and right temporal scalp locations.

ily by one common genetic factor; only for the frontal Fp1-Fp2 combination was there also a specific genetic factor. The covariances were also influenced by a common nonshared environment factor; dropping this factor in the full model led to a large increase in χ^2. However, the covariance between the left and right hemispheres

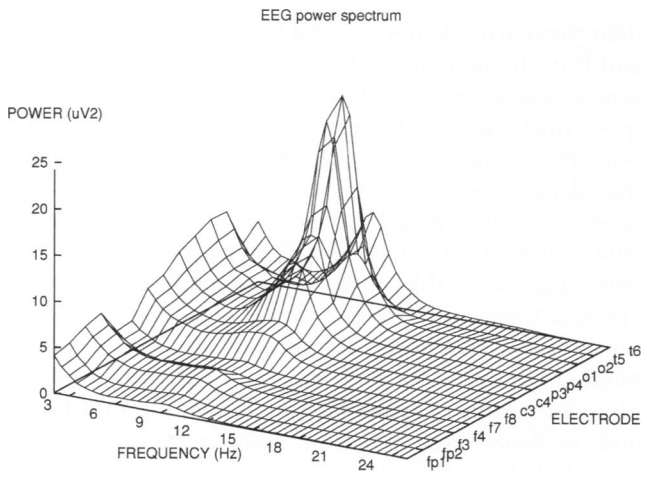

Figure 3 Absolute power of EEG spectrum, averaged over all subjects (n = 414). The amplitude (in μV^2) (*Y*-axis), frequencies (*X*-axis), and scalp locations (*Z*-axis) are given.

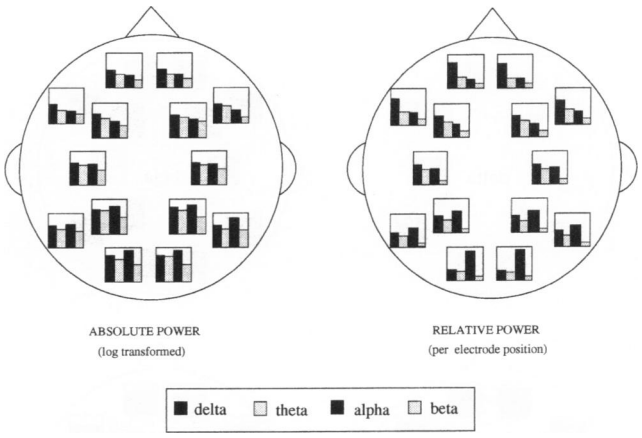

Figure 4 Mean values for absolute power (log-transformed) and relative powers for all scalp locations on the left and right hemisphere. The mean values are depicted for all four EEG rhythms (in both ideograms the sequence of the frequencies is delta, theta, alpha, and beta). The scale of the *Y*-axis is for the absolute power range 0–20 μV^2 (log-transformed values × 10) (*left*) and for the relative power range 0–.6 (*right*).

was determined mainly by genetic factors: the contribution of genetic factors was much larger (~90%, for most all brain areas) than the contribution of the nonshared environment factor (see table 1).

Multivariate analyses were performed to characterize the extent to which the same genes contribute to the observed variance of the EEG at different scalp locations. Only alpha powers were analyzed, because alpha was the dominant EEG frequency in the background EEG. The χ^2 for the full AE multivariate model for the left hemisphere was 654.02 (df = 469), and that for the right hemisphere was 581.35 (df = 469). In table 2 the genetic correlations and nonshared environmental correlations are presented. The genetic correlation is high, between all scalp locations, suggesting that, to a large extent, the same genes underlay the EEG at different scalp locations. For nonshared environmental factors, higher correlations between locations at the frontal part of the brain were found; the remaining correlations were lower than the genetic correlations.

Discussion

One of the main results of this study is the remarkable similarity of background EEG in MZ twins, for all EEG frequency bands and all brain areas. The EEGs in DZ twins showed clear familial relatedness. For most power bands and brain areas, the MZ correlations were ~.9, and the DZ correlations were half the MZ correlations. With model fitting, the genetic contributions were more precisely elaborated and tested. For most EEG powers and brain areas, the results showed mainly additive genetic effects in the 16-year-old males and females. Nev-

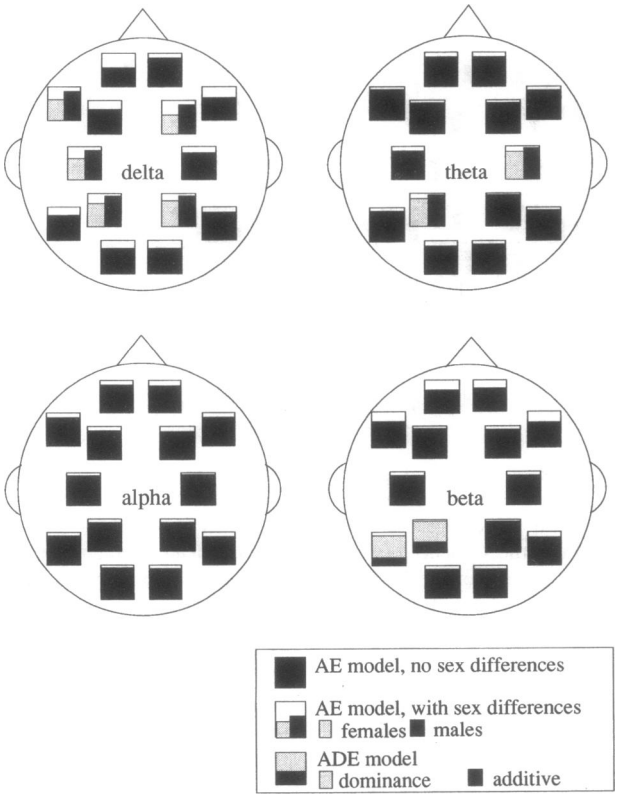

Figure 5 Proportion of variance explained by the genetic factors, for all scalp locations and four EEG rhythms (delta, theta, alpha, and beta).

ertheless, small differences in heritability existed for different EEG frequencies and brain areas.

In accordance with the typical EEG recording during rest, a large part of the EEG consisted mainly of alpha rhythm with maximum power in the parieto-occipital regions, delta with highest relative power values at frontal regions, and theta with maximum power centrally, with lower power for beta. For the delta, theta, alpha, and beta frequencies, the variance (averaged over all brain areas) explained by genetic factors was 76%, 89%, 89%, and 86%, respectively. Thus, almost no differences in heritabilities for the various EEG rhythms were present. Only for delta were somewhat lower heritabilities suggested.

The high heritabilities and MZ correlations approach the test-retest reliability normally found for EEG powers in adult subjects (Pollock et al. 1991; Salinsky et al. 1991). Thus the similarity of the EEG in a twin pair should equal the EEG similarity within a subject measured on different days. The high contribution of genetic factors to individual differences in the various EEG powers confirms the results of most earlier twin studies. However, Lykken et al. (1974) obtained, for absolute EEG powers in 37 MZ twin pairs, correlations that were comparable to our correlations, but the correlations that they measured in 27 DZ twin pairs were around 0, whereas the DZ correlations in our study were ~.5. An explanation for the low DZ correlations could be a different arousal state of the subjects, induced by the hypnotic procedure that Lykken et al. used during the EEG recording. This could cause the EEG of DZ twins to become more dissimilar while that in MZ twins remains similar. The same phenomenon is seen during alcohol intake: the EEG becomes more similar for MZ twins and becomes more dissimilar for DZ twins (Christian et al. 1988). No other twin studies have reported such low DZ correlations for EEG rhythms; in most of these studies, the correlations were ~.5, as in the present study.

For nearly all EEG rhythms and brain areas, the mode of inheritance is additive, except for power in the beta band, for which, at two scalp positions, the models indicated dominance. However, when only twins are studied, the power to detect dominance is not large.

Different brain areas reflect specific functions. The posterior areas reflect influences from visual and visuospatial functions, and the frontal areas reflect the higher cognitive functions. In addition, maturation processes have different onset and speed in different brain areas (Gasser et al. 1988; Thatcher 1992); for example, from the age of 15 years until adulthood, brain development involves mainly frontal areas (Thatcher et al. 1987; Hudspeth and Pribram 1990). Therefore, heritabilities of the EEG power could be different for the various parts of the brain. Most twin and family studies that have examined genetic influences on EEG parameters have not studied more than one brain area. The only twin study that has recorded EEG from more than one brain area was done by Meshkova and Ravich-Shcherbo (1982). In that study, alpha activity was measured in frontal, temporal, central, parietal, and occipital areas in 20 MZ and 20 DZ twins. For alpha, higher MZ correlations were found for parietal and occipital areas than for central, temporal, and frontal areas. Meshkova and Ravich-Shcherbo (1982, p. 103) suggested that the genetic influences were larger in phylogenetically older (posterior) regions: "In the more recent organs and functions the variability is higher than in the older regions, that depend on the effect of genetic factors and have become more refined by selection." However, in their study, only 20 DZ and 20 MZ twins participated. To detect significant differences in heritability among brain areas, a larger number of twins is necessary. More recently, a family study (Trubnikov et al. 1993) has estimated heritability for EEG rhythms and their topography in a sample of schizophrenic families (25 probands and 58 first-degree relatives). Additive genetic factors contributed a large part to the variance in the various EEG rhythms. Averaged over all frequency bands, the genetic influences were smaller for anterior positions, and the highest genetic contributions were found for

Table 1

χ^2 Values from Bivariate Analyses of Left and Right Hemispheres, for Each Electrode Combination and Power

		χ^2 FOR ELECTRODE COMBINATION OF						
MODEL[a]	df	F1-F2	F3-F4	F7-F8	C3-C4	P3-P4	O1-O2	T5-T6
Delta:								
AE	44	98.37	84.05[b]	79.93[b]	52.97[b]	43.14[b]	55.88	66.06
AE, one genetic factor	45	98.37	84.05[b]	79.93[b]	54.05[b]	43.43[b]	56.07	66.32
AE, only specific environment	45	386.66	212.78[b]	192.61[b]	261.54[b]	270.12[b]	254.75	103.71
Covariance (left, right)		69	92 (male), 74 (female)	99 (male), 65 (female)	94 (male), 78 (female)	96 (male), 81 (female)	80	90
Theta:								
AE	44	58.29	52.99	64.10	45.94[c]	56.15	45.35	45.76
AE, one genetic factor	45	65.39	52.99	64.10	45.94[c]	57.72	49.18	45.76
AE, only specific environment	45	319.13	182.53	115.27	213.66[c]	301.09	275.23	68.76
Covariance (left, right)		90	93	94	93	92	90	89
Alpha:								
AE	44	44.95	65.20	45.88	64.33	41.82	44.86	33.43
AE, one genetic factor	45	66.44	65.20	45.88	64.34	44.45	45.83	33.99
AE, only specific environment	45	529.72	439.72	241.65	152.56	124.04	147.43	36.38
Covariance (left, right)		88	89	91	95	95	93	89
Beta:								
AE	44	74.13	80.52	99.04	51.57	66.06	62.82	49.84
AE, one genetic factor	45	85.66	80.52	99.10	51.64	68.49	62.86	52.27
AE, only specific environment	45	199.46	172.55	157.36	152.86	173.04	175.75	56.22
Covariance (left, right)		81	93	83	94	96	92	98

NOTE.—The best-fitting models are underlined.

[a] AE is the most general model, with one additive genetic factor loading on the left and right sides, plus a specific factor for the right hemisphere. In the second model (AE, one genetic factor), the specific genetic factor for the right hemisphere is dropped. In the last model (AE, only specific environment), common environment is dropped and only specific nonshared environment is retained. Covariance (left, right) is the proportion of covariance between left and right hemispheres that is explained by additive genetic factors.

[b] Model has sex differences (df = 38, 40, 40).

[c] Scalar models (df = 43, 44, 44).

posterior positions. This agrees quite well with the heritabilities obtained in our study. The heritabilities for the different brain areas were equal for most EEG rhythms, except for delta. For delta rhythm, lower heritability was found for the anterior part of the brain. In this part of the brain, eye movements could contribute to the EEG. Eye-movement artifacts are always a problem in any attempt to quantify EEG rhythms in the anterior part of the brain. In general, the test-retest reliability is lower for this EEG rhythm (Burgess and Gruzelier 1993).

Since the introduction of quantitative EEG analysis, several developmental studies have looked for possible sex differences in EEG parameters, especially during puberty. Generally, females show an earlier pubertal growth than do males. However, most EEG studies found no large mean differences between males and females, after age 15 years. In one of the most extensive developmental EEG studies (Matoušek and Petersén 1973), relative EEG power was measured in 160 adolescents age 16–21 years. The only difference between boys and girls was an increased amount of beta activity in females. Matsuura et al. (1985) found, in the age range of 14–17 years, a higher alpha percentage in males than in females; however, Gasser et al. (1988), who studied children $\leq$17 years old, reported no sex differences for EEG power. In our group of subjects, no sex differences in mean powers were found either.

For a few electrode positions, sex differences in genetic architecture existed. Particularly for the delta band, for almost half of the electrode positions, significant sex differences were seen. For the other EEG rhythms, no sex differences in genetic architecture existed, except for theta, in which sex differences were found for two scalp locations. The heritabilities differed, only in magnitude, between males and females, with somewhat smaller heritabilities for females. Furthermore, the heritabilty differences between males and females were small. These sex differences could have arisen by chance, because many variables have been tested.

The relative contributions of genetic factors did not differ between the left and right parts of the brain; for both hemispheres, genetic factors contribute to EEG amplitude to the same extent. In addition, bivariate analyses showed that the same genes are expressed in the left

Table 2

Genetic and Nonshared Environmental Correlations between EEG Alpha Power Measured at Different Scalp Locations, Separately for Left and Right Hemispheres

A. Genetic Correlations

	Right Hemisphere						
Left Hemisphere	Fp2	F4	F8	C4	P4	O2	T6
Fp1		.98	.99	.89	.87	.85	.89
F3	.97		.99	.92	.88	.85	.90
F7	.98	.98		.91	.88	.87	.91
C3	.88	.92	.90		.93	.85	.92
P3	.88	.89	.88	.94		.92	.97
O1	.86	.86	.87	.86	.92		.93
T5	.91	.91	.91	.92	.96	.94	

B. Nonshared Environmental Correlations

	Right Hemisphere						
Left Hemisphere	Fp2	F4	F8	C4	P4	O2	T6
Fp1		.88	.80	.60	.41	.37	.46
F3	.86		.83	.74	.42	.33	.41
F7	.86	.86		.60	.36	.41	.42
C3	.45	.66	.54		.50	.23	.39
P3	.26	.33	.28	.56		.52	.67
O1	.39	.38	.44	.29	.64		.57
T5	.34	.34	.39	.45	.75	.67	

and right hemispheres, with the possible exception of the prefrontal areas.

The last question addressed is whether the same genes are expressed in the determination of the alpha rhythm in different brain areas. This analysis was restricted to the alpha rhythm because it is the dominant rhythm in resting subjects. The genetic correlations among all scalp locations were very high, indicating that the same genes are expressed in the different brain areas. No other twin studies with multivariate genetic analysis have been performed, but there is one family study (Anokhin 1987). In 45 families the alpha and beta rhythms of the EEG were measured in different brain areas. A principal components analysis was applied to the frontal, occipital, and temporal EEG electrode positions. Most of the variance was explained by a general EEG factor, with large resemblances between family relatives. This led to the suggestion that the organization of the whole-brain EEG is mainly of a genetic nature. Our results correspond with those of Anokhin (1987). Results from our multivariate analyses suggest that the same genes influence the alpha power in all brain areas.

The nonshared environmental correlations in the anterior part of the brain were also high. This probably is due to variation induced by eye-movement correction, which effect is most prominently seen in the anterior brain areas. Other high correlations were seen among posterior scalp locations. Correlations among other areas were much lower. The nonshared environment variance never explained >20% of the total variance. The nonshared environment may represent stable environment influences, which are not familiar but systematic. Thus, the individual differences in EEG activity measured at rest are determined mainly by the same genetic influences. The absence of differences in genetic influence of the various frequencies and brain areas could point to a strong correlation between the EEG and brain structure. Perhaps the EEG measured at rest is largely a reflection of the neocortical morphology, and individual differences in this morphology may be strongly influenced by genetic factors. Unfortunately, little twin research has been done on neocortical morphology (Steinmetz et al. 1994).

In summary, for 16-year-old boys and girls, individual differences in EEG activity measured at rest are determined mainly by additive genetic factors. Very little difference in the genetic contribution to the various brain areas and different EEG rhythms was found. For delta power the heritability was somewhat lower, especially in the frontal positions. Except for a few electrode positions for the delta rhythm, no evidence was found for sex differences in genetic architecture.

The high heritability seems comparable with the heritability found in other studies, although it is difficult to

compare the results, because nearly all previous studies used a small number of subjects and measured EEG at one brain area only. Also, most other studies have used adult subjects from a wide age range, whereas we have studied adolescents, in whom brain maturation is not yet completed. In our laboratory, the same design also has been employed in a study of 200 5-year-old twins (van Baal et al. 1994). In this age group the heritability for theta and alpha was smaller, though still relatively high (averaged over electrode positions, it was 81% and 79%, respectively, for theta and alpha). For these younger twins, the heritability for beta and delta was ~50%, substantially lower than that in 16-year-old twin pairs.

Finding a trait with a high heritability is one of the conditions for successful linkage between a quantitative-trait locus and that trait. The high heritability of the EEG power is a promising starting point for studying the genetic factors that determine CNS function and thereby it is possibly also a promising starting point for studying complex behaviors.

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Appendix A

Table A1

Correlations for Each Zygosity × Sex Group, for Each Scalp Location and Power

	Fp1	Fp2	F3	F4	F7	F8	C3	C4	P3	P4	O1	O2	T5	T6
Delta:														
MZM (38)	.66	.76	.82	.86	.80	.70	.88	.86	.90	.93	.78	.73	.76	.87
DZM (36)	.38	.39	.29	.25	.14	.33	.34	.33	.32	.38	.40	.41	.35	.51
MZF (52)	.50	.60	.70	.63	.53	.65	.68	.83	.74	.86	.76	.79	.74	.84
DZF (38)	.25	.28	.64	.43	.26	.19	.59	.48	.52	.54	.62	.63	.43	.57
DOS (45)	.34	.31	.44	.44	.30	.26	.47	.48	.31	.34	.35	.43	.32	.45
Theta:														
MZM (38)	.89	.91	.91	.94	.91	.90	.93	.94	.93	.94	.91	.90	.85	.87
DZM (36)	.55	.48	.43	.35	.39	.47	.46	.41	.53	.48	.57	.54	.54	.53
MZF (52)	.88	.88	.89	.89	.88	.87	.86	.88	.87	.91	.86	.89	.88	.89
DZF (38)	.55	.52	.54	.51	.58	.50	.50	.45	.52	.53	.58	.60	.54	.55
DOS (45)	.54	.57	.53	.53	.48	.55	.50	.47	.39	.38	.41	.44	.38	.37
Alpha:														
MZM (38)	.89	.88	.91	.91	.92	.90	.93	.95	.94	.93	.93	.92	.92	.84
DZM (36)	.47	.43	.51	.41	.41	.37	.49	.43	.46	.38	.46	.42	.42	.32
MZF (52)	.87	.87	.87	.88	.88	.88	.90	.92	.90	.93	.90	.88	.86	.90
DZF (38)	.50	.50	.51	.47	.57	.56	.45	.35	.40	.38	.55	.49	.43	.43
DOS (45)	.57	.56	.60	.55	.56	.53	.60	.56	.37	.37	.39	.34	.43	.43
Beta:														
MZM (38)	.87	.86	.93	.94	.81	.69	.91	.92	.97	.94	.88	.90	.90	.80
DZM (36)	.31	.34	.43	.38	.48	.37	.42	.37	.33	.34	.42	.39	.36	.43
MZF (52)	.64	.76	.90	.90	.77	.74	.93	.93	.93	.93	.86	.87	.85	.87
DZF (38)	.36	.41	.25	.13	.41	.24	.19	.12	.14	.11	.42	.36	.21	.23
DOS (45)	.36	.24	.36	.32	.25	.35	.41	.52	.33	.44	.40	.43	.26	.38

Appendix B

Table B1

χ^2 Values for All Scalp Locations and Four EEG Rhythms, for an AE model (df = 13)

	Left Hemisphere						
	Fp1	F7	F3	C3	P3	T5	O1
Delta	9.36	17.78[a]	22.15	17.18[a]	13.28[a]	26.59	16.82
Theta	16.78	10.03	7.15	12.45[b]	7.63[a]	12.67	10.06
Alpha	11.12	8.73	16.07	13.88	6.18	5.54	9.29
Beta	21.84	11.94	10.03	11.74	15.90[c]	15.36[c]	8.33
	Right Hemisphere						
	Fp2	F8	F4	C4	P4	T6	O2
Delta	10.17	14.10	7.75[a]	16.12	11.20[a]	16.56	15.85
Theta	12.61	17.19	13.24[b]	10.14[a]	13.11	10.94	9.58
Alpha	11.29	14.37	14.63	16.80	6.58	8.36	8.86
Beta	14.93	14.29	11.97	16.41	13.04	7.76	15.82

[a] The AE model with sex differences (df = 11) is the best-fitting model.
[b] The scalar AE model (df = 12) is the best-fitting model.
[c] The ADE model is the best-fitting model (df = 12).

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