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Genetic Influences on EEG Coherence in 5-Year-Old Twins

G. C. M. van Baal,[1,2] E. J. C. de Geus,[1] and D. I. Boomsma[1]

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Electroencephalographic (EEG) coherence has been suggested to be an index of the connectivity of the brain. It represents the coupling between two EEG signals from different brain areas and is mathematically analogous to a cross-correlation in the frequency domain. We obtained data from 167 pairs of 5-year-old twins to study genetic and environmental influences on individual differences in intrahemispheric coherences. Coherence was computed in the theta band (4.0 to 7.5 cycles/s) between prefrontal, frontal, central, parietal, and occipital regions during quiet rest. Univariate genetic analyses of the data showed moderate to strong genetic influences for all coherences. Broad heritabilities ranged from 30 to 71%, with a mean heritability of 49%. With one exception, no sex differences were found. Split-half reliabilities varied with interelectrode distances, ranging from .91 for the shortest distance to .62 for the longest distance. When split-half reliabilities are compared with heritabilities, the data suggest that for cortico-cortical connections between adjacent brain areas, a large part of the variance is explained by "true" environmental influences, whereas for longer connections, that is, sensory to frontal areas, the variance is mostly genetic in origin.

KEY WORDS: Brain; EEG coherence; twins; heritability; children; genetics.

INTRODUCTION

Numerous studies have demonstrated that a wide range of human behaviors is influenced by genetic factors (for reviews see Rose, 1995; Boomsma, 1993; Plomin *et al.*, 1994). Such genetically caused individual differences in behavior may be associated with individual differences in brain functioning. Genetic influences on brain functioning form a good starting point to study genetic influences on complex behavior (Lander, 1988). Brain functioning can be indexed by the electroencephalogram (EEG), which measures electrical activity of the brain. The EEG is composed of many cyclic signals of different frequencies, and spectral analysis is often used to quantify the contribution of these signals. With spectral or Fourier analysis, the signals are transformed from the time domain to the frequency domain, and a number of parameters can be obtained. A widely used parameter is the power spectrum (i.e., the amount of variance explained by each frequency component in the spectrum). In a previous study we showed that EEG power shows remarkably high heritability in children (Van Baal *et al.*, 1996). At first sight, this finding indeed seems to bridge the gap between genes and behavior, because EEG power in the broad bands has been associated with a number of temperamental characteristics, for example, with anxiety (Heller *et al.*, 1997) and intelligence (Gasser *et al.*, 1983). However, the association of EEG power with either behavior or cognition has not been unequivocal (Gale and Edwards, 1986; Anokhin and Vogel, 1996). In addition, the neural mechanisms generating the surface EEG remain enigmatic. It would

[1] Department of Psychophysiology, Vrije Universiteit, De Boelelaan 1111, 1081 HV Amsterdam, The Netherlands.
[2] To whom correspondence should be addressed. Fax: +31.20.444.8832. e-mail: gcm.van.baal@psy.vu.nl.

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be desirable to use EEG parameters that more closely reflect anatomical and neurophysiological parameters, such as axonal sprouting, synaptogenesis, myelination, and pruning of synaptic connections. Recent evidence suggests that a second parameter obtained by spectral analysis, EEG coherence, may be used to index such processes (Kaiser and Gruzelier, 1996).

EEG coherence is the squared cross-correlation between signals from two scalp locations for each component in the frequency domain. It has been suggested to measure the number of corticocortical connections and synaptic strength of connections between two brain areas (Thatcher *et al.*, 1986, 1987; Thatcher, 1991, 1994a, b). Based on the structural properties of the human cortex Thatcher and colleagues (1986) proposed a "two-compartmental" model of EEG coherence. EEG generating cells in the neocortex are either (1) pyramidal cells with long-distance loop connections (e.g., frontooccipital) of an excitatory nature or (2) highly branched stellate cells with only short-distance connections (e.g., intercolumnar) of both an excitatory and an inhibitory nature (Braitenberg, 1978; Szentagothai, 1978). The pyramidal cells act in two compartments: compartment A is composed of the basal dendrites that receive input primarily from the axon collaterals from neighboring or short-distance pyramidal cells, while compartment B is composed of the apical dendrites of cortical pyramidal cells that receive input primarily from long distance intracortical connections. Short-distance coherence between electrodes for as far as 14 cm apart can be influenced by the short fiber system, while longer-distance coherence is influenced only by the long-distance fiber system, which represent the majority of white matter fibers. In children, short-distance coherence has been found to be higher for subjects with cognitive dysfunctions compared to controls. Gasser and colleagues (1987) showed that 10- to 13-year-old mildly retarded children had higher coherences than controls. Higher short-distance coherences were also found in dyslectics (Leisman and Ashkenazi, 1980) and in Down's syndrome (Schmid *et al.*, 1992). In a population of normal children, Thatcher *et al.* (1983) showed that a negative correlation exists between full-scale IQ and short-distance coherences. Therefore, low coherence seems to be the most preferred situation. A possible explanation for these findings is that, in a normal brain, selective synaptic pruning leads to less dispersion of neural signals and, thus, lowers short-distance coherences. Intelligence may be reflected in a greater specificity of short-distance corticocortical connections, thus further lowering coherence.

The main question addressed in this paper is the extent to which the interindividual variance in short distance coherences in 5-year-old children is influenced by genetic and by environmental factors. In addition, we examine the genetic architecture of the second compartment, which is reflected in the long-distance coherences. Two previous studies of genetic influences on EEG coherence have been conducted. Van Beijsterveldt (1996) studied long- and short-distance coherences in 213 adolescent twin pairs. She reported substantial additive genetic influences on coherences in 4 broad bands and 18 electrode combinations. Heritabilities of short- and long-distance coherences appeared to be the same. For these adolescents, the mean heritability was 60%. Ibatoullina and colleagues (1994) studied heritabilities of EEG coherences of 37 5-year-old twin pairs. Familial similarities were found, although it is not clear whether these are influenced by genetic factors or whether they are due to a shared environment (common environmental effects). In the present study 70 monozygotic and 97 dizygotic twin pairs were used to estimate the contributions of genetic and common and unique environmental influences on right and left intrahemispheric coherences of resting background EEG. Since large sex differences in interconnectivity of brain areas are suggested in 5-year-olds, as reflected in mean differences in coherences (Marosi *et al.*, 1993), twins of both sexes were included to test for sex effects on heritability. Because measurement error may be a concern when studying young children, split-half reliabilities were calculated to get more insight into the actual reliability of the data.

METHODS

Subjects

The data presented in this paper were collected in a longitudinal study of genetic and environmental factors that influence neural development in early life (Van Baal, 1997). Initially, 209 5-year-old twin pairs (mean age = 5.26 years; SD = .19 year) participated. All subjects were healthy, had a normal IQ (Boomsma and Van Baal, 1998),

and had normal or corrected to normal vision. The twin pairs were registered in the Netherlands Twin Register, which contains between 45 and 50% of all Dutch twins born after 1986 (Boomsma *et al.*, 1992). Zygosity determination for same-sex twin pairs was done either by blood typing (ABO, MNS, Rhesus, Kell, Duffy, Kidd, Lutheran) or by DNA fingerprinting (N = 159). For 11 same-sex twin pairs these data were not available. These twins were assigned to a zygosity group using a discriminant analysis based on their physical appearances (hair color, hair structure, confusion by acquaintances, confusion by close friends of the family). Eighteen twin pairs had incomplete EEG data because of difficulties during the experiment. Children who feel asleep during the experiment (11) and children who showed high levels of arousal or cried (13) were excluded from further analyses. This left 167 twin pairs [33 monozygotic males (MZM), 34 dizygotic males (DZM), 37 monozygotic females (MZF), 32 dizygotic females (DZF), 31 dizygotic opposite-sex twins (DOS)] with complete data.

Procedure

Detailed procedures of data collection are described elsewhere (Van Baal *et al.*, 1996). Briefly, an electrocap with electrodes in the 10–20 system of Jasper (1958) was used to measure brain activity on 14 scalp locations during a visual oddball task and during 3 min of quiet rest with eyes open and 3 min of quiet rest with eyes closed. Vertical and horizontal eye movements were recorded for correction of the EEG signal for eye-movement artifacts. EEG was recorded unipolarly with linked ear reference according to the method described by Pivik *et al.* (1993). All electrode impedances were kept below 10 kΩ. EEG was recorded continuously on an 18-channel Nihon Kohden PV-441A polygraph. Time constants were set to 5 s; the high-frequency cutoff was 35 Hz, and the sample frequency was 250 Hz. Signals were converted with a 12-bit AD converter. This paper reports on coherence measured during quiet rest with eyes closed.

Data Quantification and Data Reduction

After removal of EOG artifacts using dynamic regression in the frequency domain (Brillinger, 1975), the EEG signal was divided into 90 2-s epochs. Epochs with clippings and with abnormal EEG patterns (detected during visual inspection) were excluded from further analysis. For every epoch and for every scalp location, the raw EEG was converted from the time domain into the frequency domain using Fast Fourier Transformation (FFT), which yielded power spectra for every electrode position and cross spectra and phase spectra for every electrode combination. The phase spectrum depicts the lead–lag relation between the signals at different scalp locations for every frequency band. Phase spectra were used to determine whether the signals of two scalp locations actually had a phase difference, because zero phase differences would point to signal transport other than via the axonal fibers. EEG coherence spectra were calculated from power and cross-spectra. Smoothed power and cross-spectra were obtained by calculating the mean of all spectra over all valid epochs (minimum number of epochs = 30). Power spectra ranged from .5 to 30 Hz, with a .5-Hz resolution. The cross-spectra indicate the covariance of two signals in a certain frequency band. Coherence spectra for every frequency band were calculated using the formula

$$\text{coherence} = \frac{[\text{cross-spectrum } (1,2)]^2}{\text{power spectrum } (1) \times \text{power spectrum } (2)}$$

where 1 and 2 refer to signal 1 and signal 2.

As is shown in this formula, coherence measures the square of the linear association between two signals and is analogous to the square of the usual correlation coefficient. Thus, coherence ranges from 0 to 1. From the coherence spectra, the mean coherence for the theta band, ranging from 4.0 to 7.5 Hz, was calculated. For children, theta is a major frequency band (Niedermeyer and Lopes da Silva, 1993). Data were transformed using the formula transformed coherence = log(untransformed coherence/1 − untransformed coherence) to obtain a normal distribution of the data (Thatcher *et al.*, 1983).

Since the majority of corticocortical connections is within the same hemisphere (Nunez, 1981), coherence was calculated intrahemispherically for the following combinations of scalp locations (depicted in Fig. 1): *short-distance coherences*—from prefrontal to frontal (Fp1–F3, Fp2–F4), from pre-

frontal to central (Fp1–C3, Fp2–C4), from central to occipital (C3–O1, C4–O2); and from parietal to occipital (P3–O1, P4–O2); and *long-distance coherences*—from prefrontal to parietal (Fp1–P3, Fp2–P4), from prefrontal to occipital (Fp1–O1, Fp2–O2); and from frontal to occipital (F3–O1, F4–O2).

Statistical Analysis

Differences in mean values of coherences between males and females and between MZ and DZ twins were tested using the ANOVA procedures from SPSSPC 5.0. Since data for twin A and twin B are not independent, cotwins of a twin pair were tested separately.

To obtain an indication of the reliability of the coherence measures, split-half correlations were calculated. Two coherence spectra per subject and per electrode combination were computed: one averaged over all odd and one averaged over all even 2-s epochs from the total EEG registrations (again with a minimum of 30 epochs per average). The correlation between the coherences of those two sets of signals provides a measure of reliability.

The observed variance in the EEG coherence was decomposed into genetic and environmental parts (Neale and Cardon, 1992), using structural equation modeling with the computer program Mx (Neale, 1994). MZ twins share all their genes and DZ twins share 50% of their segregating genes on average. The correlation between additive (A) and between dominant (D) genetic factors equals 1 for MZ twins and .5 and .25, respectively, for DZ twins. Nongenetic influences were due to common (C) and unique (E) environmental factors. Common environmental factors will make twins more alike, since they share the same effect from the environment. Both MZ and DZ correlations will become larger due to this effect. Unique environmental effects are responsible for differences between MZ twins. The correlation between the shared environmental factors is 1 in both MZ and DZ twins. Correlations for the nonshared, unique environmental influences (E) are 0 for both types of twins.

The relations between different influences on interindividual differences in a trait are used to construct a structural model to test the significance of the effects. For example, we can construct a model containing additive and dominant genetic effects and unique environmental effects, but without common environmental effects (ADE model). A number of models were fitted to the data and compared with each other: ADE, ACE, AE, and E models, with or without sex differences. Sex differences were examined in three models: (1) scalar effects sex-limitation models, in which a difference in total variance between males and females was allowed, but in which the relative contributions of A, D or C, and E were the same for males and females; (2) common effects sex-limitation models, in which the relative magnitude of genetic and environmental factors can differ between the sexes, but the same genes and/or common environmental influences are expressed; and (3) general sex-limitation models, which 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 .5. When different genes account for the phenotypic variance the additive genetic correlation in DOS pairs will be smaller than .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 sum-

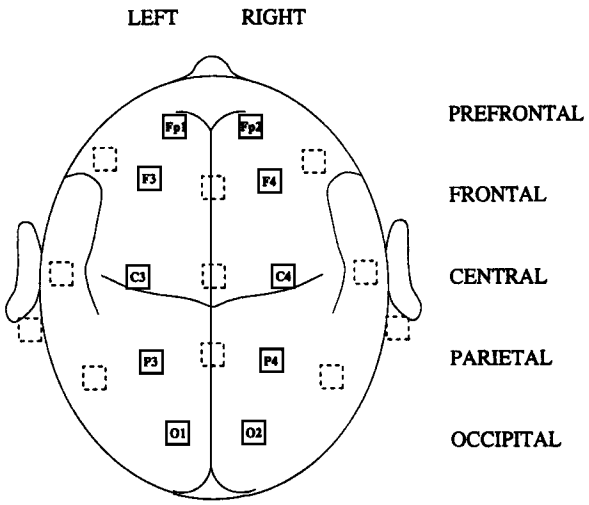

Fig. 1. EEG was measured at the following scalp locations: prefrontal (Fp1, Fp2), frontal (F7, F3, F4, F8), central (C3, C4), parietal (P3, P4), occipital (O1, O2), and temporal (T5, T6). This paper shows the results of coherences between solid squares (i.e., Fp1 with F3, C3, P3, and O1; O1 with P3, C3, F3, and Fp1; and their right hemisphere analogues).

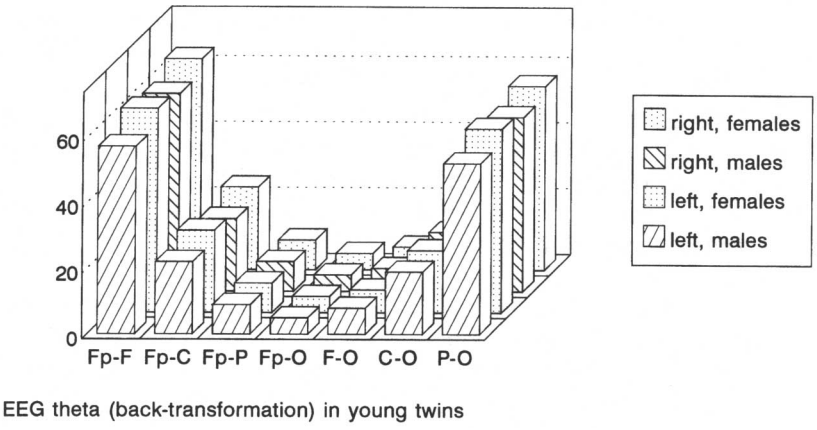

Fig. 2. For males and females, mean left and right theta coherences for seven electrode combinations within each hemisphere, with different interelectrode distances, are depicted. Fp, prefrontal scalp location; F, frontal; C, central; P, parietal; O, occipital. Mean distances between electrodes are 7, 14, 21, 28, 21, 14, and 7 cm, respectively. Untransformed means are shown.

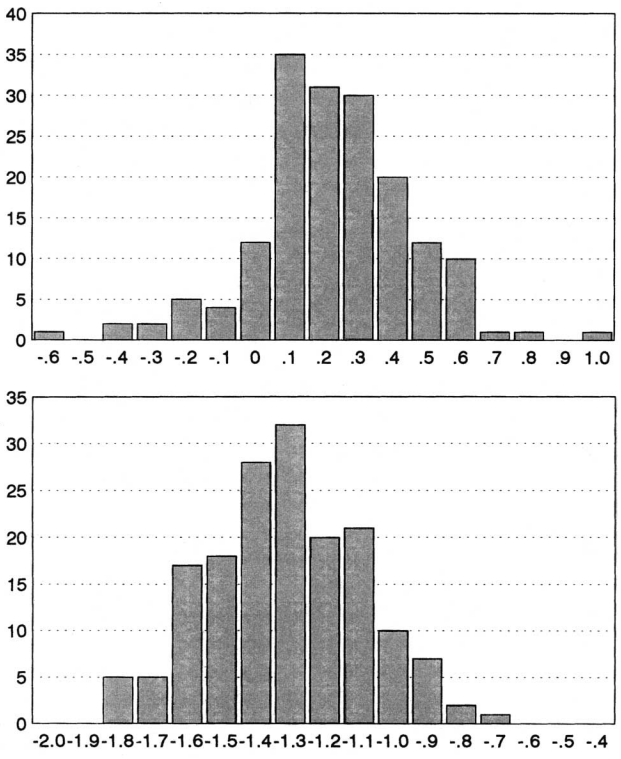

Fig. 3. Variability of transformed coherences [$y = \log(x/1 - x)$] for short distance (about 7 cm; Fp2–F4) and for long distance (about 28 cm; Fp2–O2). Although mean values are rather different, variabilities are comparable.

marized into five 2 × 2 variance–covariance matrices. The models outlined above were fitted to these matrices. The values of the factor loadings of A, D or C, and E, expressed as parameters a, d or c, and e, and their confidence intervals were estimated by maximum likelihood. The fit between the observed data and the model was assessed by χ^2 tests. To compare the fit of two models, hierarchic χ^2 tests were used. With these tests the χ^2 of a nested model is subtracted from the χ^2 of a more parsimonious model. This difference is again χ^2 distributed, with the difference of degrees of freedom of the two models as degrees of freedom. For the best-fitting models heritability (h^2) was calculated as the proportion of additive genetic variance of total variance, and d^2 as the proportion of nonadditive genetic variance of total variance. For heritabilities, 80% maximum likelihood-based confidence intervals (Neale and Miller, 1997) are provided.

RESULTS

Figure 2 shows mean coherences in the theta band for different electrode distances, for left and right hemispheres, and for males and females. The larger the distance between the electrodes, the lower the coherence becomes. This might imply lower variability on larger distances, which could indicate that variability can hardly be decomposed at the largest distances. However, Fig. 3 demonstrates that variability of the log-transformed coherences is very much alike for short and for long distances.

Mean values for coherences were larger in females for a number of corticocortical connections.

In the left hemisphere the coherences between prefrontal and frontal [twin A, $F(1,166) = 8.00$, $p = 0.005$; twin B, $F(1,166) = 7.01$, $p = 0.009$], between prefrontal and central [twin A, $F(1,166) = 6.94$, $p = 0.009$; twin B, $F(1,166) = 4.48$, $p = 0.036$], and between parietal and occipital [twin A, $F(1,166) = 5.62$, $p = 0.019$; twin B, $F(1,166) = 7.36$, $p = 0.007$] electrodes were significantly higher for females. In the right hemisphere significantly different higher coherences for females were found in twin B only, between prefrontal and frontal [$F(1,166) = 7.85$, $p = 0.006$] and between prefrontal and central [$F(1,166) = 4.18$, $p = 0.043$] electrode positions (for twin A a trend toward this effect was seen). Mean values for MZ and DZ twins were never different, and no interaction effects were found.

Split-half correlations of coherences between 14 electrode combinations are shown in Table I. Reliability becomes slightly lower with longer distances. Mean split-half correlations are .91, .86, .73, and .62 for 7-, 14-, 21-, and 28-cm interelectrode distances, respectively. This would indicate that the measurement error is larger for coherences at longer distances.

Twin correlations are also presented in Table I. As can be seen, correlations were almost always larger for MZ twins than for DZ twins, indicating that genetic influences are of importance. Differences between MZF and MZM correlations would suggest differences in heritabilities between males and females. MZF correlations seemed to be larger than MZM correlations for coherences between left prefrontal and central scalp locations (Fp1–C3) and for frontal with occipital leads (F3–O1), suggesting sex differences in heritabilities of coherences. DOS correlations were not notably lower than same-sex DZ correlations, except for coherence between the right occipital electrode (O2) and the frontal or prefrontal electrodes (F4 and Fp2). All these effects were then formally tested using model fitting.

The bottom part of Table I shows model-fitting statistics. Model fitting revealed that either an AE model or an ADE model fit the data best. A common-effects sex limitation model reached significance only once: females showed higher heritability than males for coherence between left prefrontal and central scalp locations [$\Delta\chi^2(2) = 7.86$]. No indication was found for common environmental effects. In most cases a good fit was obtained with a low χ^2 and a high p value. For coherences between nearby electrodes, an AE model was sufficient to describe the data, whereas for electrode combinations at a longer distance, dominance effects were significant, except for coherence between left prefrontal and occipital electrode positions. When dominance was included in the model, additive genetic effects were estimated to be zero, which is biologically not very plausible (Falconer, 1989).

Figures 4a and 4b show heritabilities with their 80% confidence intervals for the best-fitting models. A moderate to large part of the variance was explained by genetic factors for all electrode combinations. Coherences between adjacent electrodes (such as Fp1 and F3, or P4 and O2) showed a relatively low heritability, in combination with a high reliability. This indicates that a large part of the variance is due to unique environmental influences, other than measurement error. Longer distances, such as Fp2 with P4, or Fp2 with O2, show a relatively large heritability in combination with a somewhat lower reliability, which indicates that the reliable part of the variance is influenced for the largest part by genetic factors.

DISCUSSION

This study has determined the heritability of intrahemispheric coherences in 5-year-old children. Overall, genetic as well as unique environmental effects were important for coherences. Broad heritabilities ranged from 30 to 71%, with a mean of 49%. To date, information about genetic and environmental influences on coherence is restricted to a few studies. Ibatoullina and colleagues (1994) studied coherences in 5-year-old twins (20 MZ and 17 DZ) and found evidence of familial influences. The study was too small to distinguish between genetic and shared environmental influences. Their results certainly allow for the genetic influences found in the present study. The only other study known to us, a large twin study in 213 adolescent twin pairs (Van Beijsterveldt, 1996), also showed significant genetic influences on EEG intrahemispheric coherences. Heritabilities were slightly higher than in the present study: about 60%. This difference in heritability between children and adolescents, albeit small, agrees with the idea that, depending on age, genetic control on EEG traits may vary. The mean values of both short-range and long-range coherence in the adolescents were lower

Table I. Reliabilities, Twin Correlations, and Model-Fitting Results of Intrahemispheric Theta Coherences[a]

Mean coherence in theta: left hemisphere, eyes closed							
	Fp1–F3	Fp1–C3	Fp1–P3	Fp1–O1	F3–O1	C3–O1	P3–O1
Distance	7 cm	14 cm	21 cm	28 cm	21 cm	14 cm	7 cm
Reliability							
Split-half	.91	.86	.76	.68	.74	.86	.93
Twin correlations							
MZM	.51	.38	.69	.48	.38	.53	.32
DZM	−.02	.09	.12	.23	−.13	−.06	−.24
MZF	.55	.70	.72	.56	.66	.64	.48
DZF	.39	.14	.07	−.04	.06	.16	.13
DOS	.28	.12	.11	.22	.02	.32	.17
Model fitting							
Best model	AE	AEsex	ADE	AE	ADE	AE	AE
χ^2	14.96	9.02	8.60	6.51	9.18	9.63	25.77
df	13	11	12	13	12	13	13
p	.310	.620	.737	.925	.688	.724	.018
$\Delta\chi^2$	0.37	3.21[b]	7.00	2.29	6.08	2.45	1.78
Estimates							
h^2	.49	.33/.70[c]	.00	.50	.00	.55	.30
d^2	—	—	.71	—	.56	—	—
Mean coherence in theta: right hemisphere, eyes closed							
	Fp2–F4	Fp2–C4	Fp2–P4	Fp2–O2	F4–O2	C4–O2	P4–O2
Distance	7 cm	14 cm	21 cm	28 cm	21 cm	14 cm	7 cm
Reliability							
Split-half	.89	.86	.74	.57	.69	.85	.92
Twin correlations							
MZM	.50	.34	.61	.43	.45	.44	.55
DZM	−.15	.12	.16	.05	−.18	.19	.04
MZF	.26	.34	.59	.57	.56	.65	.51
DZF	.37	.25	−.12	.06	.10	.11	.00
DOS	.26	.24	.09	−.18	−.30	.08	.05
Model fitting							
Best model	AE	AE	ADE	ADE	ADE	AE	AE
χ^2	25.21	18.51	18.84	11.13	13.33	6.29	10.55
df	13	13	12	12	12	13	13
p	.022	.139	.092	.518	.346	.935	.648
$\Delta\chi^2$	0.00	0.00	7.40	4.67	5.25	1.59	2.10
Estimates							
h^2	.33	.33	.00	.00	.00	.51	.43
d^2	—	—	.59	.49	.46	—	—

[a] For the left and right hemispheres and for seven electrode combinations, the following information is given: distance is the approximate distance between the electrodes; reliability is calculated using the split-half approach; twin correlations are given for five sex × zygosity groups; model-fitting results indicate the best model, with its χ^2, df, and p value. $\Delta\chi^2$ is the difference between an AE and an ADE model without sex differences, df = 1. For the best-fitting model, parameter estimates of additive heritability (h^2) and dominant heritability (d^2) are given. When dominance is not included, d^2 is indicated by a dash.

[b] Fp1–C3 sex difference, $\Delta\chi^2(2) = 7.86$; the difference from the ADE model has df = 2.

[c] Male/female.

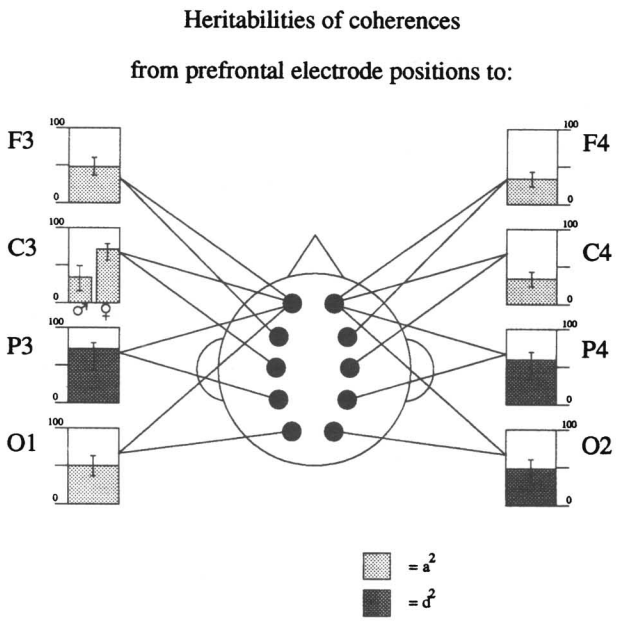

Fig. 4a. Corticocortical coherences with prefrontal electrodes: heritabilities (h^2) and relative influences of dominance (d^2) are shown with their 80% confidence intervals.

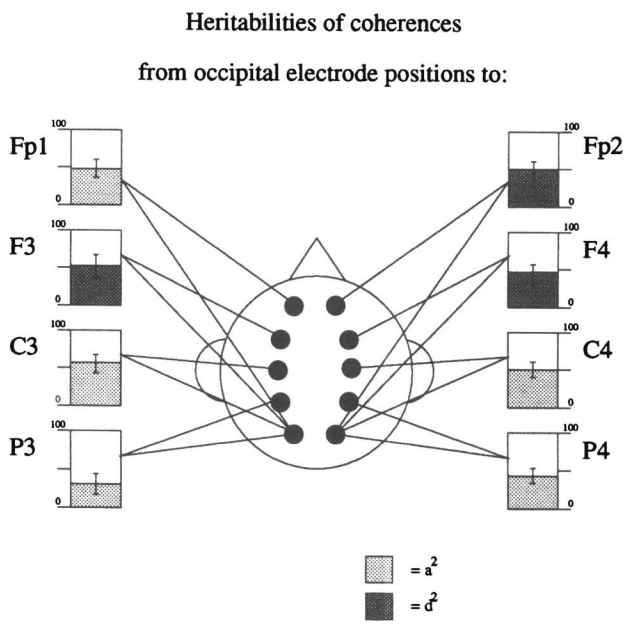

Fig. 4b. Corticocortical coherences with occipital electrodes: heritabilities (h^2) and relative influences of dominance (d^2) are shown with their 80% confidence intervals.

than coherences in children. The difference in coherence between adolescents and children suggests that both short- and long-range coherences decrease with increasing cognitive maturation.

We chose to study the genetic architecture of EEG coherence, because it has been empirically associated with cognitive abilities and because clear theoretical notions have been put forward to link this trait to structural aspects of the brain. The interpretation of EEG coherence in terms of corticocortical connectivity is based largely on a nonlinear mathematical wave model by Nunez (1981) that attempts to describe the synchronicity between neural generators in terms of anatomical parameters, such as synaptic delays, conduction velocity, and corticocortical fiber length. This model has been integrated by Thatcher *et al.* (1986; Thatcher, 1994a, b) with specific knowledge about the structure of the human neocortex. He distinguished a short-distance fiber system, which gradually becomes less important with increasing distance, and a long-distance fiber system. Kaiser and Gruzelier (1996) hypothesized that changes in short-range coherence are associated with changes in synaptic density: further differentiation of local neural circuitry through pruning leads to a smaller dispersion of neural signal and thus increased coherence. Long-range coherence, on the other hand, would be lower if the number of synaptic contacts is smaller, although this may be offset by a larger degree of myelination.

In spite of its theoretical elegance, the evidence for the existence of separate compartments influencing coherence is incomplete. Several aspects of our results are in good agreement with these theoretical notions about the difference in short and long range coherence. First, when phenotypic correlations between long- and short-range coherences were computed, low correlations between different coherences were found (e.g., between short-distance coherence for Fp1–F3 and long-distance coherence for Fp1–O1, the correlation was .13). This suggests that different genetic and environmental factors underly short- and long-range coherence. Second, it is remarkable that, although long-distance as well as short-distance coherences are influenced to a large degree by genetic factors, the long-distance coherences seem to be controlled to a large extent by nonadditive genetic factors, whereas short-distance coherences are controlled by additive genetic factors only. A similar pattern was found by Ibatoullina *et al.* (1994).

However, some caution is in order. Using only twin data it is difficult to distinguish between additive and dominant genetic effects (Eaves, 1972), which is also reflected in the somewhat larger confidence intervals of d^2 in the ADE models presented in this paper. Furthermore, we tentatively attributed the nonadditive genetic variance to dominance, although it is possible that other forms of nonadditive gene action may have caused (at least part of) this nonadditive variance. Lykken (1982) suggested that EEG power is influenced by emergenic effects, that is, a complex interaction of a number of genes on different loci, a mechanism which may also explain the pattern of twin correlations for EEG coherence. However, Eaves (1988) indicated that it is more likely that digenic epistasis explains a pattern of twin correlations like those we found for long range coherences. The finding of nonadditive genetic effects on long-range coherences ties a nice connection between physiology and genetics. If connections between two brain areas are a result of an interaction between these areas, this could be reflected in the nonadditive genetic variance that was found for these coherences.

A last important difference between short- and long-distance coherences is the difference in the heritability that was observed after reliability was taken into consideration. Reliability of a trait is the upper bound for heritability, so that a lower reliability would result in a low heritability. We computed split-half correlations and found that these were high for short-distance coherences (.91) and became somewhat lower with increasing distances (.62 for longest distances). Split-half reliabilities for coherences were about the same as those measured in a group of adolescent twins in our laboratory (Van Beijsterveldt, 1996). Heritabilities roughly were the same or became even larger with increasing distance. This indicates that, compared with long-distance coherences, for short-distance coherences a smaller part of the reliable variance is genetic. Genuine environmental effects play a larger role for short- than for long-distance coherences, suggesting that, at this age, long-axonal connections between sensory and (pre)frontal areas are more genetically determined than connections between adjacent intrahemispheric cortical areas.

Since large sex differences in interconnectivity of brain areas are suggested in 5-year-olds (Marosi *et al.*, 1993), we tested for sex differences in mean coherences. In our study slightly higher mean intrahemispheric coherences in females than in males were found, mainly in the left hemisphere and only for short-distance coherences. Marosi and colleagues (1993) also found higher coherences in females, but mostly in the right hemisphere. The twins used in our study (aged 5 years) were younger than the children used in their study (aged 7.6 to 13.3 years). Thatcher *et al.* (1987) suggest that the left hemisphere matures earlier than the right hemisphere. If short-distance coherence reflects increased differentiation of the local circuitry, our data and those of Marosi may point to a maturational lead in girls.

EEG coherence can be regarded as an index for both structural and functional brain characteristics, but can also be influenced by task-related aspects (French and Beaumont, 1984). The structural baseline depends on the anatomical features of the brain, that is, the number and synaptic strength of corticocortical connections. However, the actual "state" of coherence can change according to the demands of the task or the emotional state of the subject. The twins in this study were measured in the same resting state, and children with extreme behavior, such as crying or sleeping, were discarded from the analyses. In that way we hoped to lower the variance due to the emotional state of the subjects. In spite of these precautions, it is still possible that, apart from estimating heritabilities of corticocortical connections, we are also estimating heritabilities of the emotional state of the subject. A further concern in the interpretation in coherence is the confounding by volume conduction. Coherence can be due in part to conductivity through other tissue than axonal fibers, such as skull or blood. Although skull is a poor conductor, blood may serve as a good conductor (Nunez, 1981). Coherence would thus become a function of skull size and blood supply. However, when volume conduction is responsible for coherence between two scalp locations, phase differences between these signals will be zero. When signals are transported via the much slower medium of myelinated axonal fibers, phase differences will reflect the velocity of this electric transport and will become larger than zero. Phase differences were always nonzero for the intrahemispheric coherences reported here.

In conclusion, our data clearly showed moderate to high genetic influences on intrahemispheric coherences in 5-year-old children. The genetic in-

fluences seem to be most important in long-distance coherences, whereas unique environment, other than measurement error, plays a significant role in short-distance coherences. Finding genes that influence a clearly genetic trait such as intrahemispheric coherence can eventually shed some light on the proteins produced by these genes and, additionally, the mechanisms through which coherence and, later on, behavior emerge.

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