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Longitudinal Study of Genetic Influences on ERP–P3 During Childhood

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The P3, a component of the event-related potential, is an electrophysiological reaction of the brain to an event. It has been extensively studied as an index of attentional and memory processes in humans, and the substantial individual variation in its amplitude and latency has been related to individual differences in cognitive function and ability. Little is known about the relative contributions of genetic and environmental influences to the individual differences in this event-related potential component. Furthermore, it is unclear whether and how these influences vary during maturation in childhood. In this study, P3 was measured twice in 164 young twin pairs, once at age 5, and once at age 7. Participants performed a visual oddball task with 100 nontarget and 25 target stimuli. P3 amplitudes and latencies were obtained at 6 scalp locations (C3, Cz, C4, P3, Pz, and P4). Results show an effect of age (smaller amplitudes and shorter latencies at age 7 than at age 5), stimulus type (larger amplitudes and longer latencies for targets than for nontargets), and electrode location (largest P3 amplitude at Pz, longest P3 latencies at central electrodes). No gender differences were found for mean amplitude or latency. A genetic model was fitted to the data that decomposed the reliable variances and covariances of P3 at ages 5 and 7 into genetic and environmental parts. A significant part of the true variance in P3 latency was genetic. Heritabilities were 13% to 78% at age 5 and 36% to 99% at age 7. Heritabilities for P3 amplitude in response to targets were low (0%–19%) but high in response to nontargets (36%–86%) at both ages. At most scalp locations, the same set of genes influenced latency and amplitude from age 5 to age 7. An additional genetic factor common to the latency of targets and nontargets was found at age 7, but only for Cz and P3 scalp locations. We conclude that

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genetic influences are responsible for the stable interindividual differences in P3 latency and nontarget P3 amplitude and that these influences are largely established at age 5.

Converging evidence from animal studies (Zecevic, Bourgeois, & Rakic, 1989) and morphometric, positron emission tomography (PET), and magnetic resonance imaging (MRI) studies in humans (Chugani, Phelps, & Mazziotta, 1987; Huttenlocher, 1979; Huttenlocher, De Courten, Garey, & Van der Loos, 1982; Jernigan et al., 1991) suggests that early brain development from childhood to adolescence is characterized by a gradual decrease in gray matter and an increase in white matter. The decrease in gray matter, starting at about 4 years (Pfefferbaum et al., 1994), is thought to reflect a pruning of synaptic contacts, such that only connections incorporated into functional networks survive, and random connections are eliminated. The increase in white matter may reflect the ongoing myelination of the many cortico–cortical connections. Although this general pattern of brain development occurs in all children, the extent and the time-course of myelination as well as synaptic pruning show clear differences between individuals (Benes, Turtle, Khan, & Farol, 1994; Huttenlocher et al., 1982). It is likely that these individual differences in the maturation of the brain affect the development of interindividual differences in cognitive functions as well as overall behavior. In an attempt to trace these effects, previous studies have used the electroencephalogram (EEG) as a noninvasive index of brain development (Friedman, 1991; Stauder, Molenaar, & Van der Molen, 1993; Stauder, Van der Molen, & Molenaar, 1995; Thatcher, Walker, & Guidice, 1987). Generally, their results supported the existence of both continuous maturation and discrete growth spurts in EEG activity.

At present, the nature of individual differences in these maturational changes in brain function is unclear. To what extent the same or different genetic factors are expressed with the passing of time is unknown, as is the extent to which the timing of their expression is modified by environmental effects (e.g., those related to family or school). Using genetically related participants, such as twins, it is possible to distinguish between genetic and environmental contributions to interindividual differences. Monozygotic (MZ) twins share all their genetic material; dizygotic twins share, on average, 50% of their genes. If differences in event-related potential (ERP) parameters are larger within DZ twin pairs than within MZ twin pairs, then the greater resemblance in ERP phenotype of MZ twins is caused by their greater genetic resemblance. This study is part of a research project in which 209 twin pairs were tested when they were 5 years old and when they were 7 years old. The sample included MZ and DZ male and female same-gender and DZ opposite-gender twin pairs. By including opposite-gender twins in the sample, possible gender differences in the stability of genetic and environmental factors could be tested as well. Collecting data repeatedly in time on the same twins made it possible to address

the question of whether heritability changes as children grow older and enter a different maturational stage. More interesting, longitudinal data from twins can distinguish between genetic and nongenetic causes of phenotypic stability and estimate the extent to which the covariance across time is caused by the same genes operating at different time periods (Boomsma & Molenaar, 1987; Eaves, Long, & Heath, 1986). This means that changes in the genetic and environmental effects on maturation across time can be studied directly.

In a previous part of this research project, we showed high heritabilities of absolute and relative EEG alpha and theta power during quiet rest in 5-year-old twin pairs (van Baal, De Geus, & Boomsma, 1996). Because the ratio between EEG alpha and EEG theta is generally seen as an index of brain maturation (Petersén & Eeg-Olofsson, 1971), our findings suggested that the individual differences in some aspects of brain maturation are largely under genetic control. However, the exact relation between EEG power, cognition, and behavior is unclear. EEG rhythms are driven mainly from subcortical areas and may bear little relation to the functional development of the cortical cell layers. In contrast, development of stimulus-evoked changes in EEG, the so-called ERPs, appears to closely mirror the time course of development of gray and white matter (Courchesne, 1977; Courchesne, Elmasian, & Young-Courchesne, 1987). The P3 (also known as P300) shows particular promise. It can be reliably evoked, even in young children, by a simple oddball paradigm. The P3 is a positive going wave in the ERP that occurs 300 ms or more after stimulus presentation. It is a late, endogenous component in the ERP, and is associated with the information-processing demands of the task rather than with the obligatory activation of neuroanatomical structures in the stimulated primary pathways, which is indexed by the earlier, exogenous components. The latency of the P3 (i.e., the timing of its peak) provides a measure of mental processing speed that is independent of behavioral responding (Donchin, Karis, Bashore, Coles, & Gratton, 1986). Latency gradually decreases with age until young adulthood (Courchesne, 1978, 1979, 1990; Friedman, 1992; Polich, Ladish, & Burns, 1990). Individual differences in P3 latency have been suggested to be related to faster processing speed in various tests of cognitive function (Emmerson, Dustman, Shearer, & Turner, 1990; Ladish & Polich, 1990). P3 amplitude is sensitive to task relevance and (subjective) probability of the stimulus and is suggested to be proportional to attentional resources invested in the maintenance and updating of working memory (Polich, 1996). Indeed, larger P3 amplitude has been associated with superior memory performance (Fabiani, Karis, & Donchin, 1990; Noldy, Stelmack, & Campbell, 1990). Taken together, these findings suggest that knowledge about the genetic architecture of P3 contribute to the theory of individual differences in cognitive maturation.

Genetic and environmental influences on individual differences in P3 amplitude and latency have been investigated in a small number of studies only (for a review, see van Beijsterveldt & Boomsma, 1994). Most studies used a twin design to estimate heritability. Surwillo (1980) studied P3 latency in an auditory oddball task

in 6 MZ twin pairs and 6 unrelated pairs of children, ages 9 to 13 years, and found evidence for genetic influences. O'Connor, Morzorati, Christian, and Li (1994) studied P3 amplitude and latency in an auditory oddball task in a group of adult twins (59 MZ and 39 DZ). They found significant genetic influences on P3 amplitude, but not on P3 latencies. In two smaller studies with adult participants (Polich & Burns, 1987; Rogers & Deary, 1991), genetic influences on both amplitude and latency of an auditory P3 were suggested. A family study also provided evidence of familial resemblance in P3 latencies and amplitudes in both auditory and visual tasks (Eischen & Polich, 1994). However, that study included only 10 families, so no distinction could be made between common environmental and genetic influences. A study of P3 amplitudes and latencies in adolescent twins using a visual oddball task was conducted in our laboratory (van Beijsterveldt, 1996). In that study, 213 adolescent twin pairs participated. Strong genetic influences were shown on amplitudes for nontarget stimuli. For target amplitudes, results were less clear, but familial resemblances were found. No genetic influences on P3 latencies were observed. Recently, Katsanis, Iacono, McGue, and Carlson (1997) reported on a P3 study in 64 adolescent MZ and DZ twin pairs. The study included an easy and a difficult visual oddball task. Genetic influences for P3 amplitudes were found in both tasks, but for latencies genetic influences were only significant in the difficult task.

Except for Surwillo's study (1980), none of these studies included children. Because P3 changes in amplitude and latency from childhood to adolescence, results from adult genetic studies cannot simply be extrapolated to children. More important, no study has attempted to assess the changes in genetic contribution to P3 across childhood. This is surprising because cognitive abilities show remarkable changes in genetic architecture as children grow up. When children are young, individual differences in intelligence and verbal and nonverbal abilities are more determined by shared environment than by the genotype. When children get older, the influence of heritability increases. Between ages 6 and 12, heritability reaches its adult values of 50% to 60% (cf. Boomsma, 1993; McGue, Bouchard, Iacono, & Lykken, 1993; Plomin & Rende, 1991; Thompson, 1993). Because P3 is related to cognitive development (Courchesne, 1990; Stauder et al., 1993, 1995), we would expect the changes in genetic contribution to cognitive abilities to coincide with changes in genetic contribution to the P3. The age range chosen in this study, from 5 to 7, seemed optimal to detect a sudden shift in genetic contribution. In the longitudinal data from the Colorado Adoption Project (Cherny & Cardon, 1994), heritability of childhood IQ increased after age 4, with new genetic factors emerging somewhere between age 4 to 7. In addition, in middle childhood most children show a qualitative change in cognition referred to within a Piagetian framework as a shift from the preoperational to the operational phase (Piaget & Inhelder, 1969).

Although the longitudinal design is an essential and valuable aspect of this study, it also induces specific methodological problems. In children, the P3 amplitude and latency are more difficult to detect than in adult data, because the P3 wave is much broader. This may result in less reliable P3 measures, which may strongly affect estimates of heritability. Also, because the reliability of the P3 wave improves with age, comparing data from age 5 to 7 may yield spurious increases in heritability that are due solely to a decrease in measurement error, because in the usual genetic model, measurement error is included in the environmental component. Thus, a large error component will lead to a low heritability (h^2), because h^2 is the ratio of genetic variance over total variance. In this article, a model is used in which genetic and environmental influences and measurement error are distinguished based on multiple ERP measures, and h^2 can be estimated for the reliable part of the phenotypic variance.

METHOD

Participants

Within a 1½-year interval, 209 healthy Dutch twin pairs participated twice (i.e., 96% of the twins were tested within 1 year and 6 months). Participants were 5 years old at the first measurement occasion ($M = 5$ years and 3 months, $SD = 0.2$ years), and around 7 years old at the second measurement ($M = 6$ years and 10 months, $SD = 0.2$ years). All twin pairs were registered in the Netherlands Twin Register, which contains between 50% and 60% of all Dutch twins born after 1986 (Boomsma, Orlebeke, & van Baal, 1992). Zygosity for the same-gender twin pairs was determined either by blood typing (ABO, MNS, Rhesus, Kell, Duffy, Kidd, Lutheran) or by DNA fingerprinting ($n = 159$ pairs). No blood typing or DNA analyses were available for 11 same-gender twin pairs, who were assigned to a zygosity group based on their physical appearance by means of a discriminant analysis.

No complete data were available for 17 twin pairs, because they did not participate the second time. Data from 26 twin pairs were discarded from further analysis because of difficulties during data collection at the first or second measurement occasion (i.e., the child could not perform the task, or ERP signals were distorted due to movement artifacts). One twin had an extremely high P3 amplitude, and another twin had an extremely long P3 latency. These two twin pairs were also discarded from the analyses. This left 164 twin pairs with complete data: 33 monozygotic males (MZM), 37 dizygotic males (DZM), 33 monozygotic females (MZF), 31 dizygotic females (DZF), and 31 dizygotic opposite-gender twins (DOS). No significant differences in IQ, gender, or age were found between children who participated once and children who participated twice. Twins were measured on the same time of day (morning or afternoon) and had normal or corrected to normal vision. Participants were rewarded with a small present.

Procedure

The protocol was the same on both measurement occasions. After the twins and their parents arrived in the laboratory, the protocol was explained to them, and height, weight, and head circumference were measured. Next, one of the twins participated in the electrophysiological experiment, while the other twin was given an IQ test in an adjacent room (Boomsma & van Baal, this issue). To measure EEG activity, an electrocap with electrodes in the 10–20 system of Jasper (1958) was attached while the child watched a video. Four tin electrodes for eye movement recordings and two ear electrodes as references were also attached. Electrode impedance was kept below 10 kΩ. Testing took place in a dimly lit, electrically shielded, sound-attenuated cabin with intercom facilities. Participants lay on a bed and watched a black-and-white 25 × 30 cm monitor, approximately 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. This article presents the ERP data acquired during the oddball task.

Task

Participants performed a visual oddball task that consisted of 125 stimuli with line drawings of dogs as nontargets (n = 100) and line drawings of cats as targets (n = 25; Snodgrass & Vanderwart, 1980). Pictures were pseudorandomly distributed and presented on a black-and-white monitor. Build-up time of the pictures on the screen was less than 20 ms, and stimulus duration was 100 ms. After one or more short practice series (15 trials with 4 targets), five sets of 25 trials were presented (number of targets for the five sets: 6, 3, 8, 4, and 4). Participants were instructed to silently count the targets and report the result for each set. Interstimulus intervals varied (but were the same for all participants) and ranged from 1.5 to 2.0 sec (with a mean of 1.75 sec). During the interstimulus interval (ISI), a fixation point was shown, and each participant was instructed to look at it.

Data Quantification and Data Reduction

EEG was recorded continuously on an 18-channel Nihon Kohden PV–441A polygraph. Time constants were set to 5 sec, low pass filter was 35 Hz, and sample frequency was 100 Hz. Signals were converted with a 12-bits AD converter and sent to a PC for offline processing.

EEG electrodes were placed at the following scalp locations: frontal (F7, Fz, F8), central (C3, Cz, C4), parietal (P3, Pz, P4), occipital (O1, O2), and temporal (T3, T4, T6). Linked earlobes were used as references according to the method described by Pivik et al. (1993). Briefly, we used two preamplifiers with high input

impedance for each of the reference electrodes and linked the output electrically. By linking the ears this way, we prevented the effects of possible imbalances in electrode impedance introduced by the electrical double layers. Vertical eye movements were measured at infra and supraorbital sites in line with the pupil of the left eye; horizontal eye movements were measured at the outer canthuses.

P3 amplitude and latency were calculated by selecting time series of 50 ms prestimulus and 1000 ms poststimulus. Single-trial EOG artifacts were removed using dynamic regression in the frequency domain (Brillinger, 1975), and trials with clippings or large shifts in voltage were excluded from further analysis. Remaining trials were then averaged, resulting in averaged ERP wave forms per participants for targets and nontargets. Because averaged ERPs were flattened due to latency jitter, a Woody filter (window 350 to 900 ms) was used (Woody, 1967). The highest point in a window 450 to 750 ms (at first measurement) or 400 to 600 ms (at second measurement) of the Woody-filtered wave form was automatically scored as the peak of the P3 wave. All signals and peak scorings were then visually checked and adjusted, if necessary. P3 amplitude was defined as the difference in voltage from baseline to peak, and P3 latency was defined as the time from stimulus onset to peak.

Statistical Analysis

Differences in mean values. Multivariate analyses of variance (MANOVA, SPSS–PC) were used to test for differences in mean values of P3 amplitude and amplitudes between genders (men or women), zygosities (MZ or DZ), stimulus types (targets or nontargets), scalp locations, and ages (5 or 7 years). All analyses were conducted separately for both twins of a pair (first and second borns), because due to the genetic relatedness of a twin pair, the data of the two children of such a pair are not independent. A one-way analysis of variance was used to test for birth order effects on P3 latency and amplitude.

Reliability measures. Reliability of the nontarget amplitude and latency was estimated using a split-half approach. This method provides a coefficient of internal consistency. In addition to calculating an ERP averaged over 100 trials, we calculated two averaged ERPs over 50 trials (even numbered and odd numbered). In both signals the P3 peak was picked using the same procedure as in the original ERP that was averaged over all trials. The correlation between the amplitudes (or latencies) of those two signals provides a measure of reliability.

Stability measures. Test–retest correlations between the first and second measurement (1½-year interval) were computed to obtain information about stability in time of P3 amplitudes and P3 latencies for targets and nontargets.

Genetic analyses. Observed phenotypic variance (*Vp*) in P3 amplitude and P3 latency can be decomposed into genetic (*Vg*) and environmental variance. Two sources of environmental variance can be distinguished: common environmental variance (*Vc*) and unique environmental variance (*Ve*). Common environmental variance is due to a shared environment within the family. Unique environmental variance results from influences that are unique to a person and often also includes measurement error (Neale & Cardon, 1992; Plomin, DeFries, McClearn, & Rutter, 1997). The total variance thus equals: $Vp = Vg + Vc + Ve$.

To decompose the observed phenotypic variance into these components, data of genetically related participants are needed. We analyzed data of MZ and DZ twin pairs reared together. Because MZ twins share all their genes and are raised in the same family, the covariance between MZ twins is composed of all genetic and common environmental variance: $Cov_{MZ} = Vg + Vc$. All differences between the MZ cotwins are due to unique environmental influences. DZ twins also are raised in the same family and therefore will share all common environmental variance. However, DZ cotwins share only half their genes on average, meaning that only half the genetic variance contributes to their covariance: $Cov_{DZ} = .5 \times Vg + Vc$. The differences between MZ and DZ covariances (or MZ and DZ correlations) thus give information about sources of variation.

An easy way to get an impression of genetic or common environmental influences is to compare the correlations between MZ and DZ twins. If both MZ and DZ correlations are not significantly different from zero, only unique environment influences the trait (E model). If both MZ and DZ correlations are different from zero, but not different from each other, then common environmental influences are present (CE model). If the MZ correlation is twice the DZ correlation, then genetic influences are of importance (GE model).

A more sophisticated way of estimating and testing the relative influences of genes and environment is by way of structural equation modeling. A model according to the formulas of variance and twin covariances given earlier can be fitted to the data. A number of models can then be tested by comparing their goodness of fit, namely GCE, GE, CE, and E models, in which *G* refers to genetic variance, *C* to common environmental variance, and *E* to unique environmental variance. *G* refers to additive genetic variance only. Dominant genetic variance, that is, variance due to interaction between alleles at the same locus, was not reported, because twin correlations did not give an indication for such effects. Models containing additive and dominant genetic and unique environmental factors were tested but never gave a significantly better fit to the data. The models can be tested with or without constraining parameters to be equal in men and women, thus testing for gender differences in the relative influences of genetic and environmental factors.

Multivariate genetic analyses. A univariate analysis that addresses the issue of heritability of a certain phenotype uses information on the resemblance

between relatives, such as was outlined previously for twins. A multivariate genetic analysis also uses the additional information in the cross-correlations (e.g., correlation between P3 elicited by targets at age 5 in Twin 1 with P3 elicited by targets at age 7 in Twin 2) to determine the extent to which genetic influences are shared by several phenotypes or are phenotype specific. Using this additional information, a multivariate design can improve the power to detect genetic or shared environmental influences. In addition, the multivariate approach provides information about the extent to which different P3 measures (e.g., in response to target and nontarget stimuli) are influenced by the same genetic and environmental influences. Finally, the approach used allowed us to correct the estimates of genetic and environmental contribution to P3 for measurement error. For the latter purpose, we calculated two averaged ERPs for nontarget trials. These two variables were used as observed phenotypes in our multivariate genetic model. This allowed us to distinguish true variance (the covariance between these variables) from variance due to measurement error (the variable-specific variance) in P3 elicited by nontargets. Assuming that the measurement errors in both stimulus types were the same, the multivariate solution also improves the estimation of genetic and common environment effects on P3 from targets.

A path diagram of this multivariate genetic model used is given in Figure 1. In this figure, the observed variables are indicated with rectangles. For both twins and both measurement occasions, three phenotypes (one target P3 and two nontarget P3s) are analyzed simultaneously. Variance of each observed phenotype for each twin at each time point consists of two parts: a true part (true P3) and a part that is due to measurement error (U). The variance of the true part can be influenced by genotype (G), by common family environment (C), and by unique environmental influences (E). For each twin, four true phenotypes are defined: P3 responses to targets and nontargets at age 5, and P3 responses to targets and nontargets at age 7. A simultaneous analysis of these four phenotypes will allow insight about the extent to which P3 responses to targets and nontargets are influenced by the same genetic factors, environmental factors, or both. Likewise, a multivariate genetic analysis will provide information about the extent to which P3 responses at ages 5 and 7 are influenced by the same genes or environmental factors. Stated otherwise, a multivariate genetic analysis will also show whether new genetic factors are expressed at age 7. We used this general multivariate genetic model to obtain estimates of heritabilities and genetic and environmental correlations between the true part of phenotypic measures. As is shown in Figure 1, the true P3 phenotype can be influenced by G, C, or E. The first genetic factor (G1) is common to all four traits, the second factor (G2) has loadings on all traits except the first one, and so on (same for C and E). When the full four-factor model is fitted to the data, the ordering of the phenotypes is arbitrary, as long as there are no gender differences in the genetic and environmental factor loadings (Heath, Cloninger, & Martin, 1994). Multiplication of the triangular matrices of genetic and environmental factor loadings gives

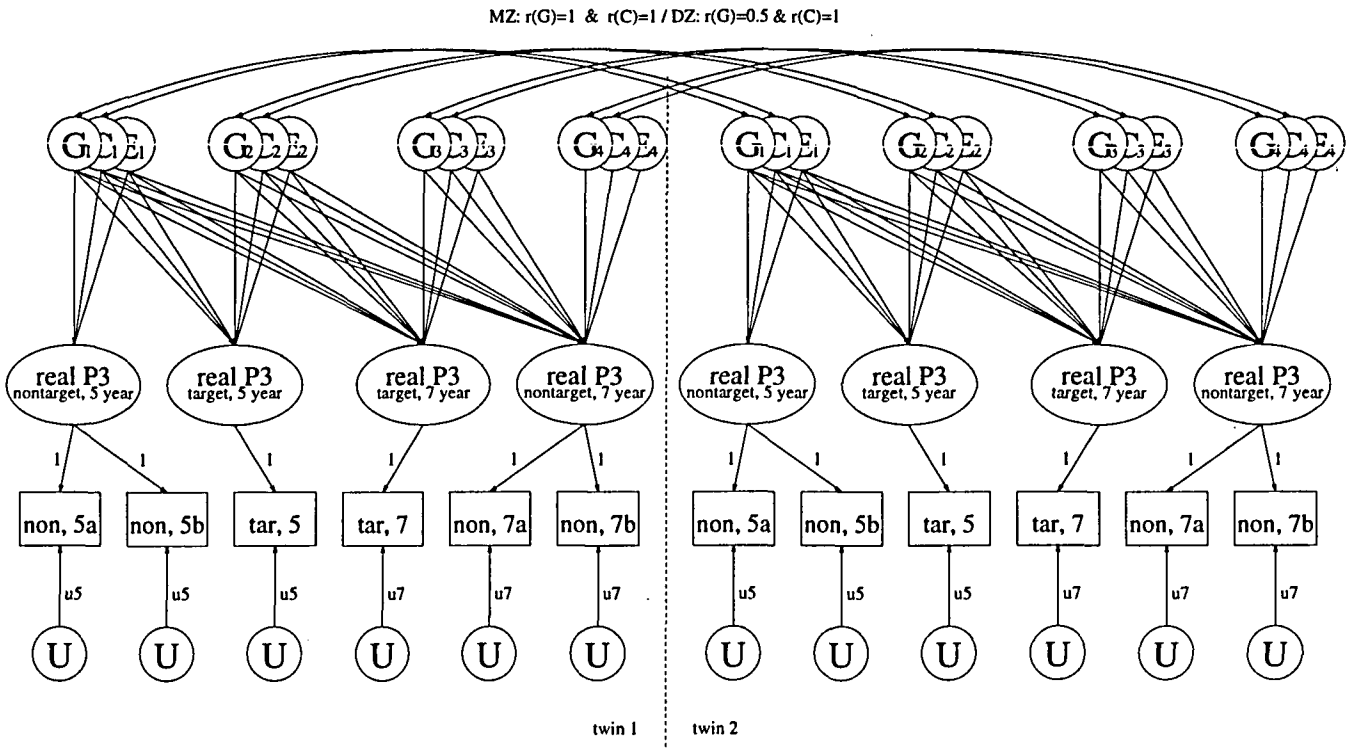

FIGURE 1 Path diagram of multivariate model. Rectangles are observed variables. For each age, three variables are available, one P3 elicited by targets and two P3s elicited by nontargets (series a and b, averaged over all odd and all even trials respectively). These are influenced by two latent factors: the true P3, and a measurement error factor (U). The true P3 is influenced by genetic (G), common environmental (C), and unique environmental (E) factors. Correlations between Gs of Twin 1 and Twin 2 are 1 for MZ twins and .5 for DZ twins. Correlations between Cs of Twin 1 and Twin 2 are 1 for all twins.

maximum likelihood estimates of genetic and environmental covariance matrices. Standardization of these matrices gives the genetic and environmental correlations between measures.

First, this model was tested allowing for differences in G, C, and E parameter estimates between male and female participants. Second, estimates were constrained to be equal for each. Third, the common environmental factors were left out to test whether they are necessary to describe the model. Fourth, an E model was tested by constraining the genetic factors to be zero. Based on the results, two other models were indicated and tested: A model with one or two genetic factors instead of a triangular decomposition was fitted to the data. The second factor could indicate age- or stimulus-specific genetic effects. For the best fitting, most parsimonious model, heritabilities and proportion of measurement error were calculated according to the following formulas:

$$\text{heritability } (h^2) = Vg / V_{\text{true-P3}} = Vg / (Vg + Vc + Ve)$$
$$\text{measurement error } (u^2) = Vu / V_{\text{observed}} = Vu / (Vu + V_{\text{true-P3}})$$

Genetic and environmental variances were estimated by Maximum Likelihood, using the computer program Mx (Neale, 1994). Data on male and female MZ and same-gender DZ twins and on DZ opposite-gender twins were summarized into 12 × 12 variance/covariance matrices. The diagonal elements of the matrices give the observed variances of the phenotype for first-born (boy in DOS) and second-born (girl in DOS); the covariance between twins is given in the off-diagonal elements. The goodness of fit was assessed by chi-square tests. A low chi-square and a high p value indicate a good fit of the model to the observed data.

Nested models were compared by hierarchic chi-square tests. The hierarchic chi-square is the difference between the chi-square of a full model and the chi-square of a reduced form of that model (e.g., a GCE model and a GE model). The degrees of freedom of the hierarchic test is the difference between degrees of freedom of the nested models. The best fitting model is the model with the most degrees of freedom (i.e., the fewest parameters necessary to describe the data), without being significantly worse than a model with more parameters. For heritabilities, 80% maximum likelihood-based confidence intervals (Neale & Miller, 1997) are provided.

RESULTS

Visual inspection of the P3 wave forms showed that in a large portion of the participants, frontal, temporal, and occipital scalp locations did not yield signals in which a P3 peak could be reliably detected in both target and nontarget ERPs. Because availability of adequate numbers of complete twin pairs is essential for

genetic analyses, we decided to analyze central (C3, Cz, and C4) and parietal (P3, Pz, and P4) electrodes only. ERPs elicited by targets and nontargets as a function of age and electrode location are depicted in Figure 2. Differences between stimulus types, measurement occasions, scalp locations, genders, and zygosities were tested. All results and analyses are reported for first-born twins, because results for second-born twins showed the same effects, and one-way analyses of variance indicated no effect of birth order. MANOVAs showed that amplitudes elicited by targets were significantly higher than P3 elicited by nontargets, $F(1, 160) = 67.21$, $p < .001$, and slightly higher at the first measurement occasion than at the second $F(1, 160) = 7.49$, $p = .007$, although the latter effect was very small (about 1 μV). Topographical differences were significant, with the Pz electrode showing the highest amplitude, $F(5, 156) = 89.43$, $p < .001$. Only one interaction effect was significant: The differences between targets and nontargets were larger on parietal scalp locations than on central locations, $F(5, 156) = 10.79$, $p < .001$. Analysis of P3 amplitude showed no effect of gender and zygosity.

Latencies for targets were longer than for nontargets, $F(1, 160) = 17.77$, $p < .001$, and shortest at parietal electrodes, $F(5, 156) = 17.63$, $p < .001$. Latencies were longer at the first measurement occasion than at the second, $F(1, 160) = 462.56$, $p < .001$. The interaction between stimulus type and measurement occasion was significant: The difference in P3 latency between targets and nontargets was larger for the first measurement than for the second measurement occasion, $F(1, 160) = 9.93$, $p = .002$. Analysis of P3 latency showed no effects of gender and zygosity.

Reliability

Split-half correlations for P3 amplitudes and P3 latencies of nontarget ERPs (i.e., the correlation between two ERPs averaged over 50 trials within one measurement session) are presented in Table 1. For P3 amplitudes the correlations are around .5 to .6, with a mean of .54 on central scalp locations and a mean of .62 on parietal locations. For P3 latencies correlations were, on average, .57 on central and .48 on parietal locations. Thus, a large part of the variance in P3 latency and amplitude in these children can be ascribed to measurement error. This is probably due to the broad P3 wave at these ages, which makes it difficult to detect its highest point.

Stability

Test–retest correlations between the first and second measurement occasion (1½-year interval) were computed to obtain information about stability of P3 amplitudes

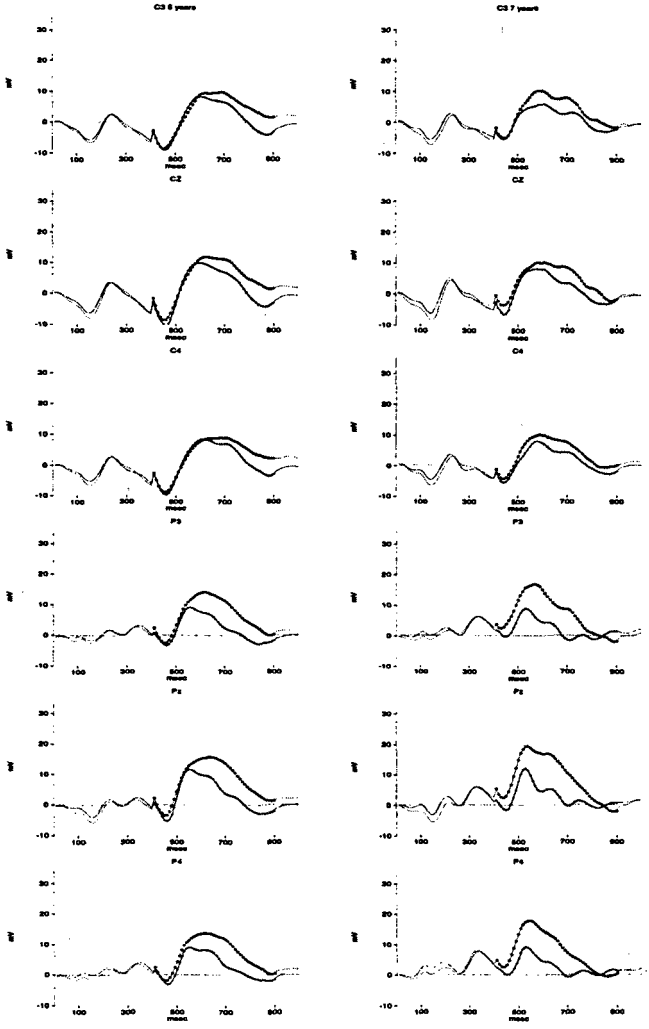

FIGURE 2 Event-related potentials (ERPs) for six scalp locations (C3, Cz, C4, P3, Pz, P4), for two stimulus types (targets and nontargets) and two measurement occasions (age 5 and age 7). The thin lines from 0 to 400 ms represent the non-Woody-filtered ERP, whereas the thicker lines from 400 to 900 ms represent the Woody-filtered ERPs, in which the P3 peak is identified. The Woody filter is applied to correct for latency jitter. The peak at the border is a result of applying the Woody filter. Lines with dots are ERPs elicited by target stimuli; lines with crosses are ERPs elicited by nontarget stimuli. Although amplitude at age 5 seems to be smaller than at age 7 (notably at Pz and P4 scalp locations for targets), this is a result of the averaging across participants. Variability between participants in latency is larger at age 5 than at age 7, and a grand average ERP then results in a broad wave with a lower amplitude. When amplitudes and latencies are obtained in each individual and then averaged, amplitude is found to be higher at age 5 compared with age 7.

TABLE 1
Split-Half Correlations for Nontargets at Age 5 Years and at Age 7 Years and Test–Retest Correlations (1½-Years' Interval) for Targets and Nontargets for Amplitudes and Latencies

		C3	*Cz*	*C4*	*P3*	*Pz*	*P4*
Amplitudes							
Split-half	Nontarget, 5 year	.53	.56	.50	.62	.66	.55
Split-half	Nontarget, 7 year	.54	.55	.58	.62	.66	.63
Test–retest	Target	.25	.30	.17	.25	.36	.29
Test–retest	Nontarget	.28	.35	.28	.35	.38	.35
Latencies							
Split-half	Nontarget, 5 year	.48	.52	.56	.52	.37	.40
Split-half	Nontarget, 7 year	.58	.59	.68	.46	.64	.49
Test–retest	Target	.18	.12	.18	.27	.17	.09
Test–retest	Nontarget	.24	.29	.17	.11	.24	.11

Note. Because the calculated split-half correlation (r^2) is the reliability of half the test, a correction was applied to estimate the reliability of the whole test (Drenth, 1975) using the Spearman–Brown formula: Split-Half Reliability = $2 \times r^2 / (1 + r^2)$.

and P3 latencies (see Table 1). For nontarget P3 amplitudes, correlations varied from .28 (C4) to .38 (Pz). Test–retest correlations for target P3 amplitudes were slightly lower. Likewise, P3 latencies showed low test–retest correlations for both targets and nontargets. Overall, midline electrodes (Cz and Pz) showed higher test–retest correlations than did lateral electrodes for amplitude and latency.

Univariate Genetic Analyses

Observed twin correlations for P3 amplitude and P3 latency, for targets and nontargets, for ages 5 and 7 are given in Appendix A. For nontarget amplitudes, MZ correlations were generally higher than DZ correlations at parietal electrode locations, but this pattern was less pronounced at central electrode locations. For target amplitudes most correlations were low, and no consistent pattern of familial resemblance could be distinguished. Twin correlations for nontarget and target latencies were low at age 5. At age 7, moderate MZ correlations were found for nontarget latencies, which were higher than DZ correlations. For targets, correlations point to some form of familial resemblance, but the pattern is not consistent.

To make our analyses comparable to previous genetic analyses in twins (e.g., O'Connor et al., 1994; van Beijsterveldt, 1996), a series of univariate models were fitted to these data. In these models, error variance was part of the unique environmental variance. For P3 amplitudes a model containing genetic and common environmental factors (GCE model) was never significantly better than

a GE or CE model. However, most of the time it was difficult to make a distinction between the latter two models. In general, for nontarget amplitudes a GE model fitted the data best, although a CE model also described the data better than did an E model. Heritabilities for nontarget amplitudes were about 40% at age 5 and slightly higher at age 7. For target amplitudes heritability was zero, and E models were sufficient to describe the data on both measurement occasions and for all electrodes.

For nontarget latencies at age 5, an E model was found at central scalp locations and a CE or GE model at parietal electrode locations. At age 7, nontarget latencies showed GE models for all scalp locations. Individual variability in target latencies could best be explained with a CE or GE model for the first measurement occasion and with a GE model for the second measurement occasion. At age 5 h^2 in nontarget latencies was zero on central electrode locations and about 30% at parietal electrode locations. At age 7 genetic contribution was about 40% on all electrode locations. For target latencies, heritabilities were about 20 to 35%.

Multivariate Genetic Analyses

The univariate results suggest a large contribution of unique environmental variance to individual differences in P3. The reliability data clearly suggest that this is due to high measurement error. To obtain a better estimate of the heritability of the true phenotype, the data were analyzed multivariately using a target P3 and two nontarget P3s. This allowed a distinction between variances due to the true phenotype and to measurement error.

P3 amplitude. First, a GCE model with gender differences was fitted to the data. In this model, estimates for genetic, common environmental, and unique environmental factor loadings were allowed to differ between male and female participants. Factor loadings of error variance were allowed to differ between genders and between ages. Next, we tried to simplify the pattern of genetic and environmental influences on true P3s. Testing influences on the reliable part of the variance of P3 amplitude showed that gender differences in parameter estimates were not significant (chi-squares for the comparison of nested models are given in Table 2). Common environmental influences could be omitted without significantly reducing the fit of the model. In addition, one common genetic factor was enough to explain the genetic variance in all observed variables. Omitting this genetic factor (E model) significantly reduced the fit of the model, indicating the importance of genetic influences.

The environmental triangular decomposition showed no clear pattern, and no attempt was made to reduce it. The last model constrained error variances to be the

TABLE 2
Chi-Squares for Six Electrodes, for Six Models, for Amplitudes

Amplitudes	*df*	*Δdf*	*Compare*	*C3*	*Cz*	*C4*[a]	*P3*	*Pz*	*P4*
1. CEgender	326	–	–	493.45	465.38	469.32	501.68	410.59	433.63
2. GCEno	356	30	1	515.49	478.65	487.46	521.25	438.11	458.12
3. GEno	366	10	2	515.87	481.15	490.94	524.39	438.35	461.19
4. Eno	376	10	3	544.63	521.52	533.00	570.61	493.23	510.23
5. 2G, Eno	369	3	3	516.18	483.93	499.22	525.44	439.12	462.23
6. 1G, Eno	372	3	5	518.70[b]	486.46[b]	502.91[b]	528.33[b]	439.36[b]	466.04[b]

Note. Nested models are compared using the difference between the chi-square of the model with its more parsimonious model, indicated in the Compare column. The difference in degrees of freedom is indicated in the *Δdf* column. Critical values at alpha = .05 for 3, 10, or 30 *df* is 7.82, 18.31, and 43.77, respectively. G = model containing four genetic factors; C = model containing four common environmental factors; E = model containing four unique environmental factors; 1G = models containing one genetic factor; 2G = models containing two genetic factors; gender = model in which parameter estimates are allowed to be different for boys and girls; no = model in which parameter estimates are constrained to be equal for boys and girls.

[a]The difference between chi-squares of the GEno model and the 1G, Eno model is 11.97; critical value = 12.59, with 6 *df*. [b]Chi-square of the best fitting model.

same in the boys and girls and at ages 5 and 7, except for C3 and C4 scalp location, where error variance was slightly higher at age 7. Table 3 shows heritabilities with confidence intervals of the true P3 amplitude, proportion measurement error of total variance, and factor loadings of the common genetic factor and the environmental triangular decomposition. For nontargets, the heritabilities ranged from 36% at C4 electrode to 86% at P3 electrode. Heritabilities were low for P3 amplitudes elicited by targets, ranging from 0% to 19%, and true unique environmental influences (i.e., unique environmental influences without measurement error) were high. Measurement error explained 39% to 66% of the total variance in P3 amplitude. The confidence intervals indicate that for targets genetic influences were not significantly different from zero at C3, C4, and P3 electrodes. At Cz, Pz, and P4, electrodes heritabilities on amplitudes were larger than zero, but significantly smaller than heritabilities for nontarget amplitudes. The lower heritabilities for targets can be a result of genetic variance that is lower or environmental variance that is higher in targets than in nontargets. The factor loadings in Table 3 show that both these effects are present. Squared genetic factor loadings were smaller for target amplitudes than for nontarget amplitudes, whereas squared (and summed) environmental factor loadings were larger. Because only one genetic factor accounted for all genetic variances for targets and nontargets at both ages, the genetic correlations between these variables were one: The same genes influence P3 amplitudes for targets and for nontargets, at ages 5 and 7.

TABLE 3
Results of the Best Fitting Multivariate Model of P3 Amplitude in Response to Target and Nontarget Stimuli at Ages 5 and 7 Years

		Gc	*E1*	*E2*	*E3*	*E4*	*U*	h^2	*CI*	u^2
C3										
Nontargets	5	2.59	2.24	—	—	—	4.59	.57	(.40–.75)	.64
Targets	5	0.91	2.84	3.99	—	—	4.59	.03	(.00–.17)	.46
Targets	7	1.17	1.58	1.82	4.05	—	5.21	.06	(.00–.17)	.54
Nontargets	7	3.01	0.00	1.59	0.00	2.16	5.21	.56	(.38–.74)	.63
Cz										
Nontargets	5	3.56	2.35	—	—	—	5.86	.70	(.49–.92)	.65
Targets	5	2.31	3.13	4.51	—	—	5.86	.15	(.05–.29)	.49
Targets	7	2.14	2.55	2.24	5.57	—	5.86	.10	(.01–.26)	.42
Nontargets	7	4.03	0.00	0.19	0.98	2.80	5.86	.65	(.45–.85)	.58
C4										
Nontargets	5	2.70	1.79	—	—	—	4.49	.69	(.28–.94)	.66
Targets	5	0.67	3.16	4.58	—	—	4.49	.01	(.00–.11)	.39
Targets	7	0.31	2.87	0.00	4.17	—	5.20	.00	(.00–.11)	.51
Nontargets	7	2.64	0.00	0.50	1.90	2.90	5.20	.36	(.19–.78)	.58
P3										
Nontargets	5	4.21	3.53	—	—	—	5.76	.59	(.41–.75)	.52
Targets	5	0.89	2.99	4.11	—	—	5.76	.03	(.00–.12)	.55
Targets	7	1.11	1.84	1.95	4.32	—	5.76	.05	(.00–.13)	.55
Nontargets	7	4.32	0.32	1.75	0.00	0.00	5.76	.86	(.68–.95)	.60
Pz										
Nontargets	5	5.27	2.91	—	—	—	6.00	.77	(.63–.90)	.50
Targets	5	2.55	3.59	4.97	—	—	6.00	.15	(.06–.25)	.45
Targets	7	2.46	3.60	2.11	4.59	—	6.00	.14	(.06–.24)	.45
Nontargets	7	5.20	0.00	0.00	0.00	3.03	6.00	.75	(.61–.88)	.50
P4										
Nontargets	5	3.77	3.02	—	—	—	5.94	.61	(.44–.79)	.60
Targets	5	2.01	2.03	5.30	—	—	5.94	.11	(.04–.21)	.49
Targets	7	2.27	0.42	2.60	3.93	—	5.94	.19	(.06–.35)	.56
Nontargets	7	4.70	0.00	0.00	0.82	2.37	5.94	.78	(.61–.93)	.55

Note. Factor loadings of genetic factors common to both ages and stimulus types (Gc), factor loadings of environmental factors (triangular decomposition, E1 to E4), and factor loadings of measurement error factor (U). Estimated heritabilities with their 80% confidence intervals, and percentage of total observed variance explained by measurement error are given in the last two columns. CI = confidence intervals for h^2; 5 = 5 years of age; 7 = 7 years of age.

P3 latency. Table 4 shows chi-squares for the nested models. For P3 latency, gender differences and common environmental influences were not significant in the reliable part of the model. A genetic one-factor model was sufficient to describe the data for C3, C4, Pz, and P4 location, whereas a second genetic factor was necessary for Cz and P3 electrode location. For the Cz electrode, the correlations

TABLE 4
Chi-Squares for Six Electrodes, for Six Models, for Latencies

Latencies	*df*	*Δdf*	*Compare*	*C3*	*Cz*	*C4*	*P3*	*Pz*	*P4*
1. GCEgender	326	–	–	460.51	450.18	490.30	405.41	462.46	484.03
2. GCEno	356	30	1	474.11	467.27	505.67	433.25	476.18	492.39
3. GEno	366	10	2	476.32	471.83	511.80	436.01	477.61	500.41
4. Eno	376	10	3	508.19	503.97	539.93	482.30	532.79	439.85
5. 2G, Eno	369	3	3	476.40	472.51[a]	513.87	440.88[a]	480.66	500.99
6. 1G, Eno	372	3	5	479.45[a]	482.09	521.22[a]	451.30	485.99[a]	506.19[a]

Note. Nested models are compared using the difference between the chi-square of the model with its more parsimonious model, indicated in the Compare column. The difference in degrees of freedom is indicated in the *Δdf* column. Critical values at alpha = .05 for 3, 10, or 30 *df* is 7.82, 18.31, and 43.77, respectively. G = model containing four genetic factors; C = model containing four common environmental factors; E = model containing four unique environmental factors; 1G = models containing one genetic factor; 2G = models containing 2 genetic factors; gender = model in which parameter estimates are allowed to be different for boys and girls; no = model in which parameter estimates are constrained to be equal for boys and girls.

[a]Chi-square of the best fitting model.

between targets and nontargets were almost 1 (1 and .91 for ages 5 and 7, respectively), indicating that the same genes influence variability in both stimulus types. However, genetic correlations between ages 5 and 7 were .29 for nontargets and .65 for targets, indicating new genetic influences at both targets and nontargets at age 7. For P3 electrode position the same pattern was seen: Genetic correlations between stimulus types were .97 and .98 at age 5 and age 7, respectively, but genetic correlations between ages 5 and 7 were .39 and .74 for nontargets and targets, respectively.

Table 5 depicts heritabilities with confidence intervals of the true P3 latency, proportion measurement error of total variance, and factor loadings of the common genetic factor and the environmental triangular decomposition. Based on the confidence intervals, heritabilities were always significantly larger than zero. On the whole, estimates of latency heritabilities were higher at age 7 than at age 5. For age 5 h^2 ranged from 13% to 78%; for age 7 h^2 ranged from 36% to 99%. The confidence intervals of these estimates mostly overlapped, so there do not seem to be reliable differences between latency heritabilities at ages 5 and 7. Measurement error explained 49% to 83% of the total variance in P3 latency at both ages. Although the differences between heritabilities at ages 5 and 7 are not significant, a trend for an increase with age in heritability seems to stem from an increasing genetic variance and a decreasing environmental variance with age. Measurement errors were the same for the boys and girls (except for Cz electrode location), but they were significantly larger at age 5 than at age 7, as is shown by the factor loadings of U.

TABLE 5
Results of the Best Fitting Multivariate Model of P3 Latency in Response to Target and Nontarget Stimuli at Ages 5 and 7 Years

Latency		*G1*	*G2*	*E1*	*E2*	*E3*	*E4*	*U*	h^2	*CI*	u^2
C3											
Nontargets	5	15.63	—	27.5	—	—	—	45.79	.24	(.10–.48)	.68
Targets	5	19.95	—	20.8	27.75	—	—	45.79	.25	(.12–.42)	.57
Targets	7	25.70	—	0.29	0.00	6.62	—	37.42	.94	(.78–1.0)	.67
Nontargets	7	24.71	—	0.00	0.00	24.14	0.00	37.42	.51	(.36–.66)	.54
Cz											
Nontargets	5	23.48	—	26.4	—	—	—	46.18	.44	(.23–.66)	.63
Targets	5	27.78	0.00	8.26	26.97	—	—	46.18	.49	(.22–.81)	.58
Targets	7	14.94	17.25	8.18	0.00	17.08	—	38.35	.59	(.31–.95)	.63
Nontargets	7	7.28	24.10	10.7	0.00	5.77	16.22	38.35	.61	(.39–.80)	.58
C4											
Nontargets	5	15.47	—	31.6	—	—	—	44.68	.19	(.07–.39)	.62
Targets	5	15.53	—	20.0	34.97	—	—	44.68	.13	(.03–.42)	.52
Targets	7	22.08	—	0.00	6.15	18.54	—	34.97	.56	(.26–.91)	.58
Nontargets	7	21.48	—	0.58	0.00	11.26	26.06	34.97	.36	(.10–.55)	.49
P3											
Nontargets	5	25.69	—	28.67	—	—	—	51.88	.45	(.19–.78)	.64
Targets	5	32.85	8.38	0.00	18.09	—	—	51.88	.78	(.40–1.0)	.65
Targets	7	13.70	21.03	0.00	5.77	1.80	—	43.04	.95	(.40–1.0)	.74
Nontargets	7	8.96	22.00	9.57	0.00	18.99	0.00	43.04	.54	(.31–.77)	.66
Pz											
Nontargets	5	19.36	—	21.12	—	—	—	52.30	.46	(.29–.68)	.77
Targets	5	17.87	—	19.54	21.88	—	—	52.30	.27	(.12–.51)	.70
Targets	7	23.50	—	0.00	2.05	17.65	—	35.63	.64	(.43–.89)	.59
Nontargets	7	30.37	—	0.00	0.00	0.00	15.80	35.63	.79	(.63–.94)	.52
P4											
Nontargets	5	15.02	—	26.49	—	—	—	55.38	.24	(.11–.41)	.77
Targets	5	13.94	—	23.33	17.45	—	—	55.38	.19	(.03–.43)	.75
Targets	7	19.99	—	0.00	0.19	1.38	—	44.65	.99	(.71–1.0)	.83
Nontargets	7	32.80	—	0.00	0.00	8.73	0.00	44.65	.93	(.73–1.0)	.63

Note. Factor loadings of genetic factors common to both ages and both stimulus types (G1) and an additional genetic factor mainly loading on latencies at age 7 (G2), factor loadings of environmental factors (triangular decomposition, E1 to E4), and factor loadings of measurement error factor (U). Estimated heritabilities with their 80% confidence intervals, and percentage of total observed variance explained by measurement error are given in the last two columns. For Cz, measurement errors were not the same for boys and girls at age 7. u^2 was .57 (targets) and .54 (nontargets) for boys, and .66 and .63, respectively, for girls. For purposes of uniformity, the estimates based on the model without gender differences are given. CI = confidence intervals for h^2; 5 = 5 years of age; 7 = 7 years of age.

DISCUSSION

In this article, we examine the genetic and environmental contribution to individual differences in children's P3 latency and amplitude and the changes in that contribution from age 5 to 7. In the first part of this section, we discuss briefly the main findings on heritability at both ages. In the second part, we discuss the stability of genetic factors across time.

To evoke a P3, this study used the same simple visual oddball task that was used in two previous studies of Dutch children of similar age (Stauder, 1992; Wijker, 1991). Mean values of P3 amplitude and P3 latency of the twins agreed well with those found in the nontwin children from these studies. There were no gender differences for mean values of amplitude or latency of the P3.

Multivariate genetic analyses showed that heritability for the P3 amplitude to targets was low. In contrast, high heritability of nontarget P3 was found at age 5 as well as at age 7. Two previous studies also showed higher heritability for target P3 amplitude. An auditory oddball task in adult twins estimated heritability at 41% to 60% (O'Connor et al., 1994). No data were reported on nontarget amplitudes. Using the same visual oddball as this study, van Beijsterveldt (1996) found heritability to range from 42% to 60% in a large group of adolescent twins. In agreement with our finding in children, the individual variation in P3 amplitude to nontargets was mainly genetic in the adolescents and, there too, heritability of nontarget amplitude was higher than that of the targets. The difference in heritability of targets and nontargets is intriguing. Although its impact on individual phenotypic variance was less strong in targets, the genetic factor influencing targets was the same as that influencing nontargets. This implies that the same set of neural generators are responsible for generation of the P3 wave to target and nontarget stimuli. However, the substantial difference in heritability suggests that during (attentive) processing of the relevant target, the influence of unique environmental sources increases strongly. Based on current interpretations of the P3 amplitude (Polich, 1996), these environmental influences may be related to general arousal or motivational effort to allocate attentional resources to the target stimuli. Although we deliberately chose a very simple task, the latter is far more difficult to standardize in young children than in adults.

The striking differences in heritability between P3 amplitude to targets and to nontargets have repercussions for the use of P3 amplitude as a marker for pathophysiological states. Past characterization of P3's normative values has yielded baseline measures against which deviant behaviors can be evaluated. For instance, individual differences in P3 amplitude have been used as an indicator of clinical disorders, in autism (Kemner, Verbaten, Cuperus, Camfferman, & Van England, 1994) and alcoholism (Begleiter & Porjesz, 1988; Polich, Pollock, & Bloom, 1994). Polich et al. (1994) conducted a meta-analysis on 22 studies that showed that relatives of alcoholics demonstrated smaller P3 amplitudes than did controls. The

strongest effects were found for young boys (younger than 18). This may indicate that P3 amplitude has a predictive value as an index of susceptibility for alcoholism. Inasfar as this susceptibility has a genetic nature, our results suggest that the P3 to nontargets may be a better marker than that to targets, at least in young children. Stated otherwise, linkage studies aimed at finding the locations for genes influencing P3 generators might best use the P3 amplitude to nontargets as the quantitative trait rather than the P3 to targets.

There were no differences in heritabilities for P3 latency in response to targets and P3 latency in response to nontargets. Speed of target and nontarget processing appeared to be influenced strongly by genetic effects. This contrasts with the results of two other large twin studies on P3 that did not find evidence for heritability of P3 latency in adults or adolescents (O'Connor et al., 1994; van Beijsterveldt, 1996). A reason for this discrepancy is provided by the study of Katsanis et al. (1997). In that study, P3 latency was found to be influenced by genetic factors in the difficult visual oddball task, but not in the easy visual oddball task. The tasks used by O'Connor et al. and van Beijsterveldt et al. may have been too easy to detect genetic influences on P3 latencies for adults and adolescents, respectively. In our study, the same oddball task was administered as in van Beijsterveldt's study. But for children it may have been more difficult, and thus genetic influences could be detected. Moreover, measurement error may have seriously affected the model fitting of the previous studies. In the latter study, split-half correlations for P3 amplitude at age 18 ranged from .67 to .88, and test–retest correlations over a 1½-year interval ranged from .62 to .81. These values agree with studies on adult P3 reliability (Fabiani et al., 1987; Segalowitz & Barnes, 1993). However, peak detection in children's ERPs may be more difficult. In this study, split-half reliabilities of P3 amplitude and latency were unacceptably low, particularly at age 5. A large measurement error can have serious implications for detecting genetic or common environmental influences on individual differences. This is reflected clearly in the differences between heritabilities from the univariate and the multivariate model-fitting analyses. In the univariate models low estimates of either h^2 or c^2 were obtained, and it was difficult to decide if the familial resemblance was of genetic or common environmental origin. In the multivariate model, however, using odd and even trials of P3 latency as two variables, the contribution of unique environment clearly decreased, yielding true estimates of heritability for the various locations of 34% on average at age 5 and 70% at age 7. The importance of genetic influences on P3 latency has in fact already been demonstrated in candidate gene research (Noble, Berman, Ozkaragoz, & Ritchie, 1994). That study showed that P3 latency was significantly longer in 10- to 14-year-old boys with the D2 dopamine receptor A1 allelle than with the A2 allelle.

The heritability of latency implies that speed of information processing in young children is to a large extent influenced by genetic factors. As with amplitude, the same genetic factor influenced targets and nontargets. In contrast to amplitude,

however, no differences were seen in heritability of target and nontarget latency. Apparently the speed of target and nontarget processing depends on the same individual characteristic. Although many genes may contribute to this processing speed, it has been argued that the A1/A2 polymorphism for the D2 dopamine receptor plays a significant role, probably by affecting the total number of D2 binding sites in the mesolimbic system (Noble et al., 1994).

Longitudinal Analyses

Apart from establishing heritability of P3 in childhood, this study aimed to detect the emergence of new environmental or genetic factors during maturation. Participants were children from 5 to 7 years of age, because this is a period in which large cognitive changes occur. Across the repeated measurements, the P3 amplitude was seen to decrease slightly at central and parietal locations. Previous studies employing simple oddball or novelty tasks in this age range have yielded mixed results. Mostly P3 amplitude is seen to decrease in childhood (Courchesne, 1977, 1978, 1983, 1990; Friedman, 1991; Stauder, 1992), although some studies have reported no change (Wijker, 1991) or even increases (Mullis, Holcomb, Diner, & Dykman, 1985; Polich et al., 1990; Taylor, 1988). However, an apparent increase in P3 amplitude with age may be caused by the age-related decrease in variability in the latency of single trials. Correcting latency jitter by means of a Woody filter, as in this study, allows for a better comparison across time. Our findings on P3 latency agreed with virtually all published reports (e.g., Friedman, 1992; Johnson, 1988; Nelson & Nugent, 1990); P3 latency decreased from age 5 to age 7. This decrease reflects an increase in information processing speed. Several studies have shown that the decrease will continue until adolescence when it reaches its final value of around 300 ms for simple tasks, or longer (even until 500 ms) for more complex tasks. Against the backdrop of this general developmental trend, children in this study exhibited large individual differences in P3 amplitude and latency decreases. As a consequence, phenotypic correlation between first and second measurements was rather low. The low stability of the P3 parameters is mainly due to measurement error but could also be affected by session-specific effects, like seasonal effects or effects due to errors in electrode placement (Polich & Kok, 1995). In addition, differences in maturation are likely to be a relevant major source. Our results suggest that the maturation of P3 is a continuous process. Exactly the same genetic factors appeared to influence P3 amplitude at ages 5 and 7. An additional genetic factor emerged only for P3 latency at Cz and P3. Generally, the genetic factor found at age 5 still had large effects on P3 latency at age 7, including locations Cz and P3.

The stability of genetic contribution to the P3 amplitude and latency was an unexpected finding. Previous research on IQ has suggested that new genetic factors emerge between ages 4 and 7 (Cherny & Cardon, 1994). Because latency has been

associated with neural speed and IQ (Barrett & Eysenck, 1992; Chalke & Ertl, 1965), we expected new genetic factors to emerge for P3 latency as well. Instead, we only found an increase in heritability from age 5 to age 7. However, in the same sample of twins we found the same pattern for IQ data (Boomsma & van Baal, this issue): an increase in genetic variance coinciding with a decrease in environmental variance. Preliminary results of a combined analysis further indicate that correlations between latency at P3 electrode and IQ are around –.19 for both targets and nontargets. This correlation emerged in spite of the large measurement error in P3 latencies. It is possible that amplification of genetic effects on neural speed, as indexed by P3 latency, precedes the increased heritability of IQ. To test this hypothesis, we need to use an extended model, which includes IQ measures and P3 measures and which accounts for measurement errors. This next step will be pursued in the future.

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Appendix A
Observed Twin Correlations for Amplitudes and Latencies Elicited by Target and Nontarget Stimuli at Ages 5 and 7 Years

	C3		*Cz*		*C4*		*P3*		*Pz*		*P4*	
	5	*7*	*5*	*7*	*5*	*7*	*5*	*7*	*5*	*7*	*5*	*7*
Amplitude, targets												
MZM	.10	.16	−.18	.27	−.04	−.05	−.17	−.02	−.30	−.12	−.02	.05
DZM	.09	.11	.14	.26	.16	.21	−.03	.26	.04	.39	−.13	.32
MZF	.51	.14	.02	.21	−.02	.13	.32	.17	.28	.23	.25	−.04
DZF	−.16	−.24	.07	−.33	.13	.05	.08	−.11	.06	−.40	.12	.39
DOS	−.11	.02	−.27	.25	−.18	.16	.00	.31	.05	.11	.04	.19
Amplitude, nontargets												
MZM	.08	.13	.34	.52	.27	.45	.45	.26	.34	.65	.49	.62
DZM	.13	.23	.36	−.31	.15	.37	.37	.02	.24	.27	.20	.16
MZF	.37	.39	.37	.44	.42	.27	.44	.50	.48	.58	.32	.59
DZF	.18	.15	.08	−.27	.27	.16	.37	.37	.17	.28	.54	.39
DOS	.39	.38	.71	.39	.36	.19	−.30	.38	.16	.28	−.13	.14
Latency, targets												
MZM	−.10	.31	.14	.36	.02	.34	.21	.19	.03	.48	.23	.45
DZM	.25	.31	.11	−.04	.23	.27	.25	.37	−.19	.19	.32	−.08
MZF	.26	.55	.28	.24	.16	.19	.33	.48	.36	.34	.16	.38
DZF	.29	.08	.17	.21	.07	.25	.32	.14	−.01	.16	.28	−.29
DOS	.06	.42	.30	.23	.38	.12	.17	.20	.26	.33	.21	.40
Latency, nontargets												
MZM	.08	.21	.10	.44	.01	.44	.29	.51	−.23	.41	−.08	.28
DZM	.19	.29	.35	.40	.34	.19	.33	.39	.24	.04	.23	.27
MZF	.18	.62	−.03	.51	.15	.42	.39	.44	.50	.59	.41	.66
DZF	.02	.20	−.13	.14	.09	.33	.41	.14	.26	.34	.26	.30
DOS	.03	.08	.15	.00	.11	.01	.03	.04	.13	.11	.43	−.08

Note. Correlations are given for six electrode locations and for five Sex × Zygosity groups.