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Genetic sources of covariation among P3(00) and online performance variables in a delayed-response working memory task

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Abstract

Genetic and environmental sources of covariation among the P3(00) and online performance elicited in a delayed-response working memory task, and psychometric IQ assessed by the multidimensional aptitude battery, were examined in an adolescent twin sample. An association between frontal P3 latency and task performance (phenotypic $r = -0.33$; genotypic $r = -0.49$) was indicated, with genes (i.e. twin status) accounting for a large part of the covariation ($> 70\%$). In contrast, genes influencing P3 amplitude mediated only a small part (2%) of the total genetic variation in task performance. While task performance mediated 15% of the total genetic variation in IQ (phenotypic $r = 0.22$; genotypic $r = 0.39$) there was no association between P3 latency and IQ or P3 amplitude with IQ. The findings provide some insight into the inter-relationships among psychophysiological, performance and psychometric measures of cognitive ability, and provide support for a levels-of-processing genetic model of cognition where genes act on specific sub-components of cognitive processes.

Keywords: P3 (P300); Working memory; Twin study; Event-related potentials; IQ; Multivariate genetic analyses; Individual differences

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1. Introduction

In an effort to unravel the pathways through which genes may exert their influence on cognitive ability, genetic studies are employing endophenotypes, or intermediate phenotypes, that reflect central nervous system activity, and that may be more directly related to the biological effects of genes, therefore providing greater power for identifying them (Almasy and Blangero, 2001; De Geus and Boomsma, 2001). There is also an increasing use of multivariate genetic techniques that not only quantify the strength of the genetic influence but also the degree of genetic covariance among phenotypes, and allow the investigation of whether the same genetic factors influence cognitive abilities at different levels of complexity. In the present study, the genetic covariation among the latency and amplitude of the P3(00) and online task performance, in a delayed-response working memory task, was examined to investigate whether individual differences in these cognitive correlates may be attributed to some common or independent genetic source. In addition, the notion that the P3 and cognitive ability, as measured by psychometric IQ, reflect contributions from a common genetic influence was explored.

Working memory involves the active maintenance and manipulation of information and underlies many higher-level functions such as planning, problem solving, reasoning and decision making (Baddeley, 1992), thereby regulating the dynamics of human cognition. Individual differences in working memory performance, largely measured with working memory span tasks, are well documented and are thought to partly explain individual differences in a wide range of cognitive tasks (e.g. Daneman and Green, 1986; Just and Carpenter, 1992; Lehto, 1996) as well as academic performance (Jurden, 1995). The large variance in working memory function between individuals is thought to be due to differences in working memory capacity or the amount of general cognitive resources that one has available to simultaneously process and maintain information (Engle et al., 1999), such that those who have greater working memory capacity, have larger working memory spans and higher cognitive performance. Strong evidence from many sources, in both humans and non-human primates, shows that working memory depends critically on the prefrontal cortex, in particular the dorsolateral prefrontal cortex, and involves a distributed cortical network encompassing both the prefrontal and posterior association areas, especially in tasks with high working memory loads (e.g. Chafee and Goldman-Rakic, 2000; Rowe et al., 2000). Differences in the activation of various areas in the network have been reported using neuroimaging (Callicott et al., 1999), and individual differences in the relative utilisation of each area, as measured by EEG, have been associated with differences in cognitive ability (Gevins and Smith, 2000).

Brain activation measured by the P3 event-related potential has also been associated with working memory function and is commonly used as a non-invasive measure of information processing (e.g. Rugg and Coles, 1995; Polich, 1998). The amplitude of the P3 is viewed as an index of context updating with larger amplitudes elicited to increased task or stimulus complexity reflecting the increased attentional resources engaged, or more generally processing capacity employed, to encode and

update working memory (e.g. Donchin et al., 1997; Fabiani and Donchin, 1995), while the latency of the P3 is used as a measure of stimulus evaluation and classification time, it being influenced by perceptual complexity and the cognitive processing demands of the task (Kutas et al., 1977; Magliero et al., 1984). In early studies, using a simple oddball task, no consistent relationship between P3 amplitude and cognitive functioning was demonstrated but several of these studies found there was an association between P3 latency and cognitive ability with shorter latencies being associated with higher ability (Egan et al., 1992; Howard and Polich, 1985; O'Donnell et al., 1992; Polich and Martin, 1992; Polich et al., 1983, 1990). In a review of the P3 it was suggested that the strongest associations between P3 latency and cognitive ability were found for those tests that tap processing capability, in which speeded allocation and maintenance of resources is required (Polich and Kok, 1995). However, recent studies using complex tasks have demonstrated an association between P3 amplitude and cognitive ability but no relationship between P3 latency and either task performance or cognitive ability. In a five-choice reaction time (CRT) task larger P3 amplitudes were associated with higher working memory reading span scores (Nittono et al., 1999), and in an n-back working memory task, in which P3 amplitude decreases with working memory load, P3 amplitude was found to be positively correlated with cognitive ability (WAIS-R) (Gevins and Smith, 2000). P3 latency elicited in both these tasks was not associated with cognitive ability. There have also been reports of a negative correlation between P3 amplitude and cognitive ability (Houlihan et al., 1998; Mc Garry-Roberts et al., 1992; Pelosi et al., 1992a,b), and a positive association between P3 latency and cognition (Houlihan et al., 1998), leading to the conclusion that the association between P3 and cognitive ability is dependent on the type of task, with processing requirements influencing the precise relationship.

The extent to which the covariation between the P3 and cognitive ability is genetically mediated has been briefly explored in one study. In a sample of 30 MZ and 34 DZ twin pairs using an oddball task, Katsanis et al. (1997) found P3 amplitude was both moderately heritable, in agreement with earlier studies (Eischen and Polich, 1994; O'Connor et al., 1994; Rogers and Deary, 1991), and positively correlated with IQ (WAIS-R) (0.20 to 0.28). However, after partialling out the variance in P3 amplitude due to IQ, it was found that the MZ correlation remained higher than the DZ correlation, indicating that the greater similarity for MZs was not attributable to their greater similarity in mental ability, and that the genetic influence on P3 amplitude was independent of that of IQ. While more recent twin studies using large samples and genetic modelling, have confirmed that there is a substantial genetic influence on P3 amplitude (Van Beijsterveldt et al., 1998, 2001) and P3 latency (Wright et al., 2001), there have been no studies that have extended this initial investigation of Katsanis et al. (1997) using multivariate genetic techniques to investigate the extent to which heritable effects on P3 amplitude or P3 latency are shared with that of cognitive ability.

The objectives of the present study, therefore, were to examine in a large sample of adolescent twin pairs, whether individual differences in either the amplitude or latency of the P3 component, elicited in a delayed-response working memory task,

were related to (1) performance on the task, and/or (2) general cognitive ability (psychometric IQ). It examined whether any associations among the cognitive correlates were due to common genetic or environmental factors, or whether there was a genetic influence on P3 amplitude or P3 latency that was independent of task performance or general cognitive ability. The delayed-response working memory task is moderately cognitively demanding, requires focused attention and the manipulation and storage of the location of a target stimulus in working memory. Large individual differences in task performance are found for this task. It was predicted that high performing individuals would demonstrate a larger P3 amplitude, reflecting the availability of more cognitive resources for encoding the target stimulus, a shorter P3 latency, reflecting faster encoding and efficiency in processing. It was further predicted that a genetic influence would mediate a significant part of the covariance among the variables.

2. Method

2.1. Participants

Participants (525 females, 498 males) included 474 twin pairs, of which 75 pairs included an older or younger sibling, with a mean age of 16.3 (0.5 SD) years (range 15.4–20.1 years). The twin pairs included 218 MZ (114 female, 104 male) and 256 DZ (61 female, 61 male, 134 opposite sex) pairs. Zygosity was determined by analysis of nine independent highly polymorphic DNA markers and cross-checked with blood group results (ABO, Rh, MNS) and/or phenotypic data (eye, skin and hair colour, height and weight) giving an overall probability of zygosity of greater than 99.9%. All participants had normal or corrected vision (better than 6/12 Snellen equivalent) and had no history of head injuries, neurological or psychiatric conditions. Participants were instructed to avoid consuming caffeine-containing foods or drinks for 2 h before their visit and no participants were currently taking prescribed medication with central nervous system effects. Written, informed consent was obtained from participants and their parents and all data were treated confidentially.

2.2. Procedure

Participants were part of an ongoing twin study using a range of measures to explore genetic influences on individual differences in cognition. We have previously reported the magnitude of the genetic influence on the P3 (Wright et al., 2001) and working memory performance and IQ (Luciano et al., 2001) in a sub-set of the sample used in the present study. The P3 was elicited during a delayed-response working memory task, with performance on the task measured simultaneously, in a session lasting approximately 90 min. This was either preceded or followed by a session of similar duration in which psychometric IQ was measured using the Multidimensional Aptitude Battery. Co-twins attended together but were tested

separately, with the order of sessions based on birth order and counterbalanced across twin pairs. Siblings of co-twins were tested on a separate day.

2.3. Delayed-response working memory task

The task required participants to focus on a black fixation spot (0.5° visual angle), in the center of a computer screen, and use their peripheral vision to note the location of a target 'soccer ball' (1.5° visual angle) that was flashed briefly (150 ms) on the screen, 250 ms after fixation onset, and on an annulus (9.25° radius) from the fixation point. After a short delay (1 or 4 s), signaled by the disappearance of the fixation, participants showed they remembered the location of the soccer ball by lifting their hand, resting on a 5×5 cm response pad placed centrally in front of them, and touching, with a pencil shaped pointer, the position on the touch sensitive screen. Visual fixation was required to be maintained while the fixation spot was present, and responses were required to be prompt (150–1500 ms post fixation offset) and within a 2° radius of the target center. Randomly interspersed with the memory trials were an equal number of sensory (control) trials in which the peripheral target remained present throughout the delay and response interval (i.e. identical to memory trials except that target position did not have to be remembered). On 50% of both memory and sensory trials, a distractor identical to the target was briefly (150 ms) presented peripherally, 300–700 ms after target onset. Distractors occurred on the same 9.25° annulus but not within a 15° radius of the preceding target. Participants received a monetary reward dependent on performance—2–10 c per correct trial (graded on pointing accuracy) with incorrect trials incurring a penalty of 5 c. After each trial, feedback was shown on the screen showing the amount of money won. The total amount of money won, indicating overall performance, was used as the performance measure.

Following training and practice on the task, participants completed 432 trials (6 blocks of 72 trials). Testing took place in an electrically shielded, sound attenuated cubicle with the light level set to low. The computer monitor was positioned approx. 45 cm in front of the participant, with the mid-point of the screen just below eye-level. Screen background was dark grey and intensity was adjusted so stimuli could be clearly distinguished with minimal after-image effects. A black hood with a 205 mm diameter hole in the middle was fitted so that targets at all locations were an equal distance from the edge of the screen.

2.4. ERP recording and measurement

The ECI-Electrocap was used to record from 15 sites (Fp1, Fp2, F7, F3, Fz, F4, F8, C3, Cz, C4, P3, Pz, P4, O1, O2) referenced to linked ears. EOG was recorded from the supra-orbital ridge and the outer canthus of the left eye and all electrode impedances were maintained below 5 kohms. EEG signals were band-pass filtered (0.01–100 Hz) and amplified with Grass amplifiers, and sampled at 500 Hz from 100 ms prior to fixation onset to 200 ms post fixation offset. ERPs were derived from

correct trials without excessive artifact or eye movements (over 50 μV RMS), and eyeblinks were removed as in our previous studies (Geffen et al., 1997).

Following artifact rejection, trials were averaged using a pre-target baseline of 350 ms, collapsed over trial type. The rationale for collapsing over trial types was based on inspection of grandmean waveforms (Fig. 1) that showed the P3 was of similar amplitude and latency for the four trial types. Memory and sensory trials are indistinguishable for the first 150 ms (post-target onset), and can only be discriminated either when the target has been extinguished (memory trials) or when it is estimated that the target has been on longer than 150 ms (sensory trials). Similarly, memory and sensory trials with and without a distractor are indistinguishable in the first 300 ms post-target onset as distractors were presented 300–700 ms post-target. Preliminary analyses, using the first 50 twin pairs, showed the P3 to memory and sensory trials to be the same amplitude and latency, suggesting the cognitive demands and stimulus salience in the two trials is the same at this point, in which the location of the target is perceived, visuo-spatial information is encoded, and attention is maintained centrally in anticipation of responding.

To aid in identification of the latency of the P3 peak, averaged waveforms were digitally filtered with a low-pass triangular filter (5 Hz), and a computerised program used to locate the largest positive peak within the latency window 150–450 ms post-target. This window was chosen following inspection of the grandmean waveforms that showed a positive component to be elicited around 300 ms and showed no other positive peaks were elicited in this window. The program divided the search window into sub-windows of 10 ms. The slope of each sub-window was then determined by fitting a line of best fit (least squares approximation) to the data points in the sub-window. A peak was said to exist within two adjacent sub-windows if the slopes were of different sign. The program detected up to three peaks within the latency window. The P3 peak was then confirmed by direct visual inspection, at each of the 15 sites, by a research assistant blind to participant zygosity. P3 latency was defined as the time point of maximum positive peak amplitude, and where a peak could not be selected with a high degree of certainty peak latency was coded as missing (11–24 participants depending on site).

P3 amplitude was measured as the average amplitude in the 150–450 ms window relative to a 350 ms pre-target baseline, prior to filtering the waveforms. This measurement was adopted as the P3 peak because a number of the waveforms were above the baseline (i.e. in the negative region). With a P3 peak above baseline, it was not possible to get a valid measure of P3 peak amplitude, but it was possible to measure P3 average amplitude (relative to baseline). Preliminary analyses showed that for those participants in which the P3 peak was below the baseline (i.e. in the positive region), and therefore for whom P3 peak amplitude could be measured, that the correlation between peak amplitude and average amplitude was >0.92 at all sites.

As previously reported both P3 amplitudes and P3 latencies were highly correlated across sites within a brain region, and across proximal brain regions (Wright et al., 2001). Thus a mean P3 (average) amplitude and P3 latency for frontal and parietal

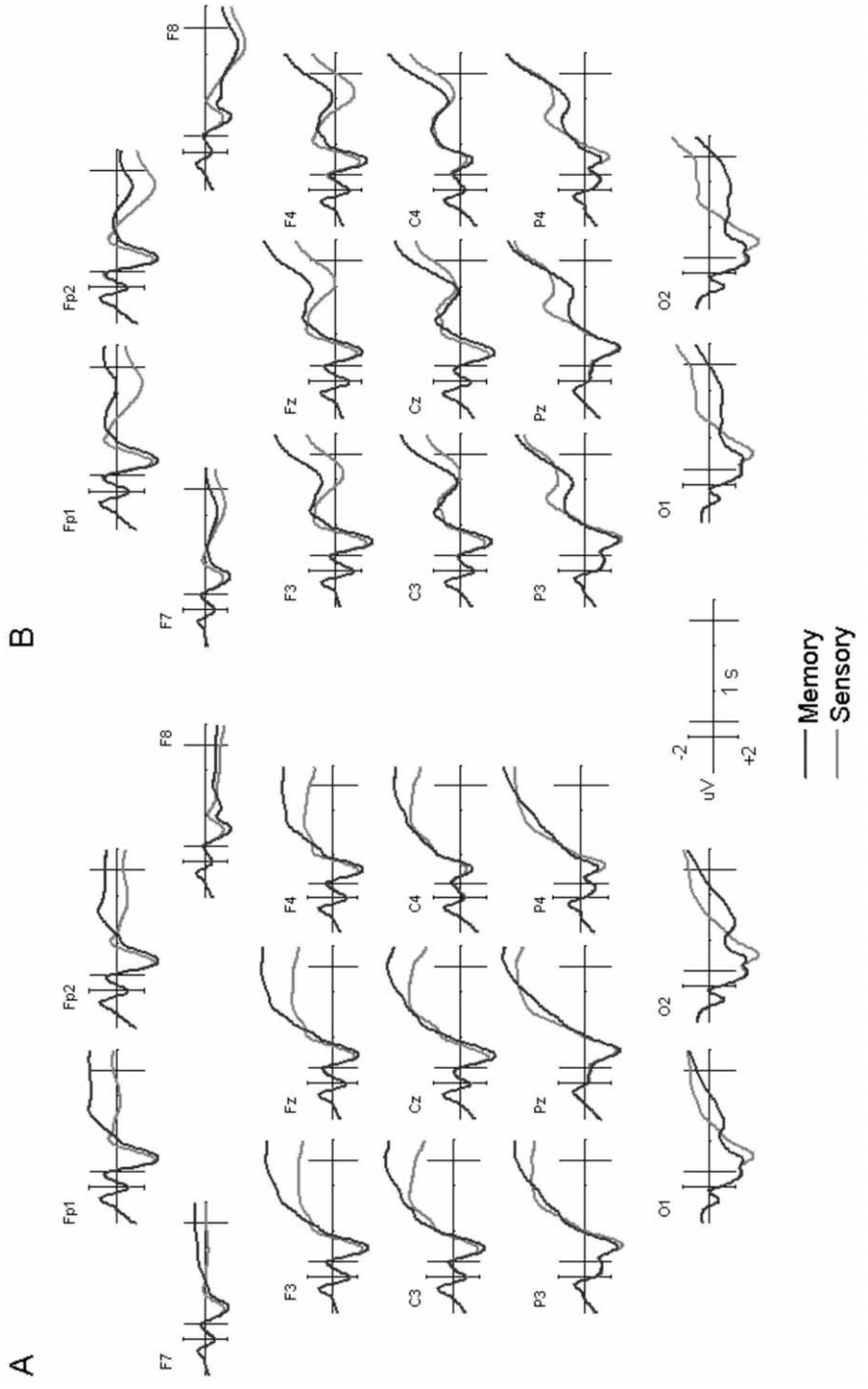
A
B
Fp1
Fp2
F7
F8
F3
Fz
F4
C3
Cz
C4
P3
Pz
P4
O1
O2
-2
uV
+2
1 s
Memory
Sensory

Fig. 1

regions was computed by averaging across the respective midline and lateral sites and used in all further analyses.

2.5. Psychometric IQ

The Multidimensional Aptitude Battery (MAB) was used as a measure of general cognitive ability. It is a group test involving multiple choice questions, and is patterned after the Wechsler Adult Intelligence Scale-Revised (Jackson, 1998). The test was taken in a quiet room in the presence of a research assistant, and was administered to each participant separately using the standard MAB instructions as specified in the manual. Three verbal (information, arithmetic and vocabulary) and two performance (object and spatial) sub-tests were used. The computerised version was used for the verbal sub-tests. For the performance sub-tests, the pencil and paper version was used for the first 326 twin pairs; this was then superceded by the computerised version when it became available. Participants were given 7 min for each sub-test with adequate time for reading instructions and practice of example questions given prior to each sub-test. They were encouraged to answer every item and were not penalised for guessing. Performance was scored by the MAB software program to yield a full-scale IQ (FIQ). Verbal and performance IQ were also scored but are not reported in this study.

2.6. Statistical analyses

Maximum likelihood (ML) analysis of the individual observations in which hypotheses about the means, variances, and covariances are tested, was used to investigate effects of birth order, zygosity (six groups) and sex using the structural equation modelling package, Mx (Neale, 1997). In addition, means and variances were tested for equality across twins and siblings, and a weighted regression parameter which tested effects of differential months of schooling on IQ was specified. As twins were tested as closely as possible to their 16th birthday there was a differential completion of months of schooling (calculated as months of schooling completed since the beginning of grade 10) between pairs that was significantly correlated with FIQ after controlling for age ($P < 0.01$). However age was not significantly correlated with FIQ when the effects of education were partialled out. In addition, as participants were tested throughout the year, an effect of season on P3 amplitude was examined, but was not significant at either frontal or parietal sites ($F(3, 961) < 1$).

Models were fitted to the data, progressing from the most saturated to the more restrictive with the fit of each model tested by the likelihood ratio χ^2-test against the

Fig. 1. (A) Grandmean waveforms for memory (solid line) and sensory (light line) trials are shown for the 15 sites. (B) Grandmean memory and sensory waveforms for trials including a distractor that was presented 300–700 ms post-target onset. The vertical bars represent target onset (0 ms), target offset in memory trials (150 ms), and fixation offset (1100 ms) for trials with a 1 s delay.

preceding, more complex model within which it is nested (Neale and Cardon, 1992). MLEs of co-twin correlations for each zygosity group were computed with means and variances constrained to be equal but including regression coefficients in the means model for any sex effects and months of schooling effects. To examine the sources and pattern of covariation among P3 amplitude, P3 latency, working memory performance and IQ, and specifically whether there are common genetic influences, a Cholesky decomposition was used. A complete decomposition for the three sources of variance—additive genes (A), shared environment (C), and individual environment (E) was specified initially. Nested AE and CE models were then compared to the saturated ACE model using the χ^2-difference test. In addition to the Cholesky, a model was fitted in which the genetic sources of variance were reduced to a 3 factor model (factor 1: latency/performance/IQ, factor 2: amplitude/performance/IQ, factor 3: performance/IQ) with specifics on performance and IQ. This model was based on the theory that P3 amplitude is a correlate of processing capability and P3 latency of processing speed. The same principles of parsimony were applied in arriving at the preferred model as described above (Neale and Cardon, 1992). ML phenotypic correlations among the six measures were calculated simultaneously with modelling any effects of sex or schooling on the observed measures, as were the genetic and environmental correlations.

3. Results

3.1. Preliminary analyses

ERP data from 59 participants (5.8%) were not included in the analyses due to technical or procedural problems (22 participants) or to excessive artifact rejection. This amount of data loss is consistent with other ERP studies. In addition software problems resulted in the loss of IQ data from two participants. Those participants with performance and IQ data but no measure of P3, were included in the analyses. All variables were normally distributed except for the task performance measure which was transformed by a reflected (maximum value+1) square root function. Univariate outliers (0–3 participants) were removed if they exceeded ± 3 standard deviations from the mean. Multivariate outliers were identified in Mx 1.50 through the %P function, which calculates likelihood statistics for each family conditional on the model. The output variable of interest was the z-score, based on the Mahalanobis distance of the data vectors (each vector represented a twin pair). Following this procedure one family was removed.

3.2. Homogeneity of means, variances and covariances

Table 1 indicates that the mean and SD for P3 amplitude and P3 latency for frontal and parietal regions, task performance, and FIQ, for both males and females. ML analysis showed that in general, means were equal across birth order and zygosity. Where inequalities were found they were for a single group and the

Table 1
Means (SD) for P3 amplitude (frontal and parietal), P3 latency (frontal and parietal), task performance, and FIQ

	Females ($N = 493–525$)	Males ($N = 443–498$)
P3 amplitude-frontal (μV)	0.25 (3.22)	1.35 (3.13)
P3 amplitude-parietal (μV)	0.34 (3.88)	2.18 (4.13)
P3 latency-frontal (ms)	292.2 (49.8)	295.2 (49.6)
P3 latency-parietal (ms)	297.9 (66.6)	310.8 (58.8)
Performance	26.14 (4.92)	26.28 (5.23)
FIQ	109.94 (12.77)	113.50 (13.15)

P3 amplitude was measured as the average amplitude in the 150–450 ms post-target window, relative to a 350 ms pre-target baseline. Frontal and parietal P3 amplitudes and P3 latencies were computed by averaging across the respective midline and lateral sites.

difference was not large (e.g. higher mean FIQ for MZ first born twin (98) compared to second (95.6) born twin). No significant differences in variance between co-twins or zygosity groups for any of the measures were indicated, and means and variances for twins and siblings were homogeneous. Mean effects for sex were found for P3 amplitude, P3 latency (parietal), and FIQ. P3 amplitude for males was marginally larger than females and males had a higher FIQ score, while females had a slightly shorter parietal P3 latency. Sex effects on the mean were taken into account in subsequent analyses by specifying a male sex deviation in the model for these variables. There was also a significant months of schooling effect on FIQ, and, therefore, mean FIQ was adjusted for months of schooling completed since the beginning of grade 10. For each of the measures, MZ correlations for females and males could be equated, and similarly, correlations of same sex DZ and opposite sex DZ twin pairs were homogeneous indicating no sex limitation of genetic or environmental influences.

3.3. Co-twin correlations

Twin correlations are shown in Table 2. For all measures, the MZ correlation exceeded that of DZ, suggesting genetic influences. The highest MZ correlation (0.81) was found for FIQ with the MZ correlation for P3 amplitude, P3 latency, and WM being of similar magnitude (0.47–0.61). DZ correlations were generally half those of MZs, and more consistent with additive genetic effects than with dominance effects. Therefore the following multivariate analysis tested for the presence of additive genetic, common environment and individual environment effects. MZ and DZ groups were pooled across sex as the MZ and DZ correlation for males and females separately showed a similar pattern to those pooled across males and females, and as the DZ opposite sex correlation was equal to the DZ same sex correlation.

Table 2
ML twin correlations (95% confidence intervals) of P3 amplitude (P3A-frontal, P3A-parietal), P3 latency (P3L-frontal, P3L-parietal), task performance, and FIQ

	P3A-frontal	P3A-parietal	P3L-frontal	P3L-parietal	Performance	FFIQ
MZ ($N = 200$-218 prs)	0.49 (0.38–0.58)	0.61 (0.52–0.69)	0.49 (0.38–0.58)	0.47 (0.36–0.57)	0.47 (0.37–0.56)	0.81 (0.77–0.85)
DZ ($N = 224$–256 prs)	0.27 (0.15–0.38)	0.25 (0.13–0.36)	0.27 (0.15–0.38)	0.16 (0.03–0.29)	0.17 (0.05–0.28)	0.49 (0.39–0.57)
MZM ($N = 92$–104 prs)	0.50 (0.34–0.62)	0.66 (0.53–0.75)	0.50 (0.34–0.62)	0.53 (0.36–0.65)	0.45 (0.29–0.57)	0.81 (0.74–0.85)
MZF ($N = 105$–114 prs)	0.48 (0.31–0.60)	0.57 (0.43–0.67)	0.48 (0.31–0.60)	0.43 (0.26–0.56)	0.51 (0.36–0.62)	0.82 (0.76–0.86)
DZM ($N = 55$–61 prs)	0.15 (−0.20–0.43)	0.41 (0.16–0.58)	0.15 (−0.20–0.43)	0.28 (0.00–0.50)	0.08 (−0.18–0.32)	0.47 (0.26–0.61)
DZF ($N = 55$–61 prs)	0.21 (−0.04–0.42)	0.11 (−0.02–0.30)	0.21 (−0.04–0.42)	0.13 (−0.09–0.33)	0.01 (−0.26–0.28)	0.52 (0.31–0.66)
DZOS ($N = 114$–134 prs)	0.33 (0.17–0.47)	0.26 (0.12–0.40)	0.33 (0.17–0.47)	0.13 (−0.07–0.32)	0.25 (0.10–0.39)	0.49 (0.35–0.59)

Table 3
ML Phenotypic correlations among P3 amplitude (P3A-frontal, P3A-parietal), P3 latency (P3L-frontal, P3L-parietal), task performance, and FIQ

	P3A-frontal	P3A-parietal	P3L-frontal	P3L-parietal	Performance
P3A-frontal	1.00				
P3A-parietal	0.52	1.00			
P3L-frontal	0.09	−0.04	1.00		
P3L-parietal	0.06	0.05	0.67	1.00	
Performance	0.04	0.14	−0.33	−0.16	1.00
FIQ	0.08	0.05	0.06	0.06	0.22

3.4. Sources of covariation among P3 amplitude, P3 latency, WM performance and IQ

ML correlations among P3, task performance and FIQ are presented in Table 3. There was a moderately strong phenotypic correlation between frontal and parietal sites for P3 amplitude (0.52) and P3 latency (0.67). However, of most interest is the phenotypic association found between P3 latency at frontal leads and task performance (−0.33), indicating those with a faster frontal P3 latency performed better on the task. There was also a significant correlation between task performance and FIQ (0.22) indicating those who performed better on the task had higher general cognitive ability. A somewhat lower P3 latency–task performance association was found at parietal sites (−0.16), and P3 amplitude was also weakly associated with task performance, and only at parietal sites (0.14). Of note is the absence of a correlation between P3 latency with FIQ, and P3 amplitude with FIQ.

To dissect the relative contributions of genes and environment to the covariation between P3 amplitude, P3 latency, task performance and FIQ, a Cholesky decomposition for three sources of variance–additive genes, shared environment, and unique (non-shared) environment (ACE model) was specified giving a fit of $-2LL_{5751} = 17\,281.6$. Dropping the genetic factors from the model (CE model) significantly worsened the fit ($\Delta\chi^2_{21} = 155.3$, $P < 0.01$ (critical value of $\chi^2_{21} = 32.67$), whereas dropping the shared environment factors from the ACE model resulted in a $\Delta\chi^2_{21} = 5.1$ (n.s.) indicating a good fit to the model. Further simplification of the additive genetic factor structure by fitting three factors (speed, capacity, performance) with specifics on task performance and IQ, did not result in a better fitting model ($\Delta\chi^2_{10} = 94.9$, $P < 0.01$, (critical value of $\chi^2_{10} = 18.31$).

The best fitting AE model is shown in Fig. 2. The first genetic factor accounted for a large part of the variance in P3 amplitude at frontal sites (49%) and some of the variance in P3 amplitude at parietal (18%), with a second genetic factor loading primarily on parietal P3 amplitude (accounted for 41% of the variance). The third genetic factor explained a substantial part of the variance in P3 latency at both frontal (49%) and parietal (29%) sites, and also accounted for 9% of the variance in task performance or 22% of the total genetic variance in task performance (i.e. 10/45). Moreover it was largely genetic factors that accounted for the phenotypic correlation of −0.33 (i.e. $0.70 \times -0.31 = -0.22$) between frontal P3 latency and

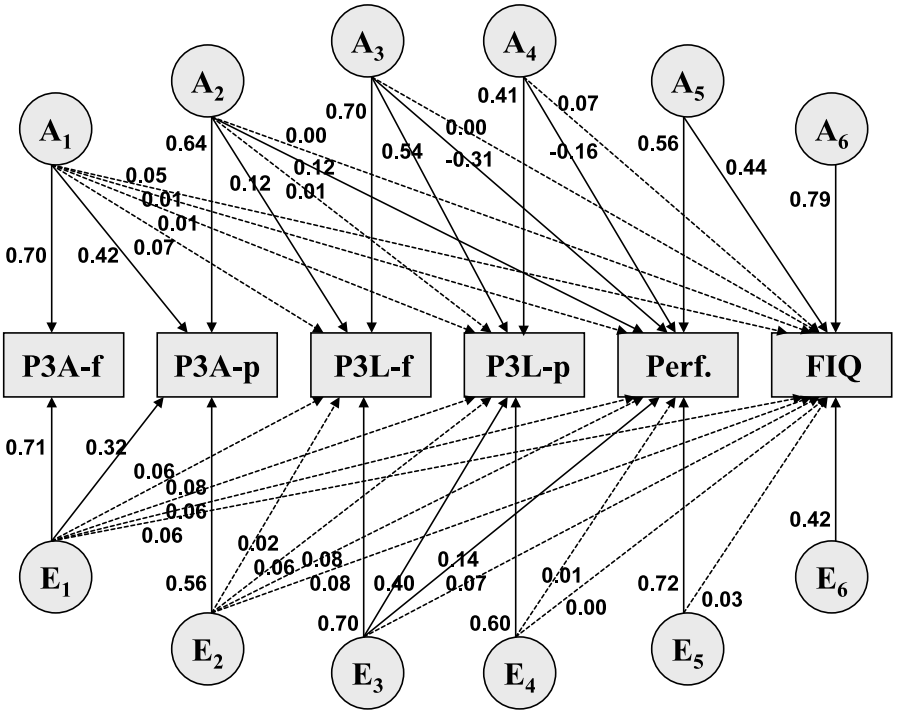

Fig. 2. Standardised path coefficients for the AE Cholesky model where A represents additive genetic factors and E represents unique environmental factors. Loadings of A and E factors that were non-significant are shown as dashed lines.

task performance. A fourth genetic factor explained the remainder of the genetic variance in parietal P3 latency (17% of the total variance) and a further 3% of the variance in task performance. A further (A5) genetic factor accounted for a significant part of the variance in task performance (31%) and 19% in FIQ (23% of the total genetic variation in FIQ), with genetic factors completely accounting for the phenotypic correlation (0.21) between task performance and FIQ (i.e. $0.56 \times 0.44 = 0.25$)). The sixth genetic factor accounted for the large remaining variance (62%) in FIQ.

In addition, specific unique environmental factors explained a large part of the variance in P3, amplitude and latency (31–50%), and task performance (52%), and a proportionally smaller part of the variance in FIQ (18%). However, correlated unique environmental effects ($> 17\%$) were only found for P3, both amplitude and latency, between frontal and parietal sites, and these were significantly smaller than the corresponding genetic cross correlations. E1 accounted for 50% of the variance in P3 amplitude at frontal and 10% of the variance in P3 amplitude at parietal sites. Similarly, E3 accounted for 49% of the variance in P3 latency at frontal and 16% of the variance at parietal sites.

Table 4
Genetic correlations (below diagonal) and non-shared environmental correlations (above diagonal) for P3 amplitude (P3A-frontal, P3A-parietal), P3 latency (P3L-frontal, P3L-parietal), task performance, and FIQ

	P3A-frontal	P3A-parietal	P3L-frontal	P3L-parietal	Performance	FIQ
P3A-frontal		*0.49*	*0.08*	*0.11*	*0.08*	*0.13*
P3A-parietal	0.55		*0.02*	*0.12*	*0.13*	*0.08*
P3L-frontal	0.09	−0.09		*0.56*	*−0.18*	*0.18*
P3L-parietal	0.01	−0.01	0.79		*−0.09*	*0.10*
Performance	0.01	0.15	−0.49	−0.23		*0.05*
FIQ	0.06	0.03	0.01	0.05	0.39	
h^2	0.48	0.58	0.51	0.46	0.45	0.81

The variation explained by genetic factors (h^2) is given in the last row. Correlations amongst measures are estimated from the full additive genetic and unique environment Cholesky model.

Genetic and environmental correlations among the six measures are shown in Table 4. The genetic correlation (−0.49) between frontal P3 latency and task performance (the extent to which the genetic deviations in P3 latency were associated with the genetic deviations in task performance) was greater than the corresponding environmental correlation (−0.18). A similar pattern was evident for the association between parietal P3 latency and task performance ($r_{\text{genetic}} = -0.23$; $r_{\text{environmental}} = -0.09$) even though the phenotypic correlation was low (−0.16), and for the task performance–FIQ correlations ($r_{\text{genetic}} = 0.39$, $r_{\text{environmental}} = 0.05$). This contrasts with the association between frontal and parietal sites, for P3 amplitude and P3 latency, for which both the genetic and environmental correlations are significant. Table 4 also shows the heritability estimates for the six measures. Heritability estimates were of similar magnitude for P3 amplitude, P3 latency and task performance (0.45–0.58), and were lower than that for FIQ (0.81).

4. Discussion

The purpose of this study was to gain a better understanding of the role of genetic influences on the covariation of some of the many sub-processes that contribute to individual differences in cognitive ability. In a large genetically informative sample, recording of the P3 was concurrent with performance measures on a delayed-response working memory task enabling a direct comparison of traditional (performance) measures of cognitive ability to psychophysiological measures of cognition. A faster P3 latency was found to be associated with better performance on the task with genes accounting for a large part (> 70%) of the covariation. However, larger P3 amplitudes were only weakly related to task performance. As previously reported (Luciano et al., 2001) there was a significant association between performance on the delayed-response task and IQ that was completely attributable to a genetic influence, but no association was indicated for either the latency or amplitude of the P3 component with IQ.

The negative association found between P3 latency and task performance indicates that participants with greater cognitive capability, who can process and evaluate the location of the target faster, were better able to perform the task. In the delayed-response task, participants are required to remember the location of a target that they are only intermittently allowed to covertly attend. They then have to shift their attention back to the central fixation and maintain focus in readiness to recall the location of the target when signaled. In half of the trials there is also the requirement to ignore a distractor that is presented soon after the target, requiring the coordination of multiple memory buffers. Thus the task demands that encoding of the target stimulus be completed quickly and suggests that task performance may be partly mediated by differences in the speeded allocation and maintenance of resources as suggested by Polich and Kok (1995). The finding is consistent with work showing that P3 latency increases as the size of the memory set increases (Houlihan et al., 1998) and the effects of ageing which show longer P3 latencies as people age and their cognitive capability decreases (e.g. Pfefferbaum et al., 1984; Polich, 1996).

Of greater interest was the finding, using genetic model fitting, that a large part ($>70\%$) of the covariation between P3 latency and task performance was due to a genetic factor. This factor explained 49% of the total variance in P3 latency at frontal sites, 29% at parietal sites, and 10% in task performance. Although 10% is on the small side it represents 22% of the total genetic variance in task performance. The genetic correlation between P3 latency and task performance, for both frontal and parietal sites, was found to be higher than the phenotypic correlation indicating that variation in genes that increase P3 latency are strongly related to the variation in genes that promote higher task performance. The magnitude of the genetic correlation was also similar to those found in psychometric studies (Finkel and McGue, 1993) between a speed factor and short term memory (0.44 and 0.50). Moreover, given that P3 latency is elicited before the behavioural response it suggests that it is the speed with which processing resources are allocated that influences task performance and not vice versa. This interpretation provides support for the limited capacity hypothesis (e.g. Jensen, 1998) in which faster speed of processing is proposed to enable better access to rapidly decaying information in working memory, whereas a slower processing speed taxes working memory capacity to maintain transient information in an accessible form. However, an alternative explanation, which also has to be considered, is a model of pleiotropy in which genes influencing P3 latency have diverse effects, and therefore may also directly influence task performance.

While P3 latency decreased with better task performance and task performance increased with higher IQ, there was no relationship found between P3 latency and IQ. Genes mediating 31% of the variance in task performance accounted for 19% of the variance in IQ, but there was also a small significant genetic influence on task performance (14%), independent of IQ, attributed to genes influencing P3 (latency and amplitude) suggesting that task performance may be influenced by two sub-components—those that share common working memory and/or attentional processes with P3, and those that share common processes with IQ. It also suggests

that the association between task performance and IQ may reflect the genetic covariation of processes that occur after the target has been encoded, such as individual differences in response processing and execution. Although the finding of no association between P3 latency and IQ is in contrast to those using an oddball task in which shorter P3 latencies were associated with some cognitive abilities (Egan et al., 1992; Howard and Polich, 1985; O'Donnell et al., 1992; Polich and Martin, 1992; Polich et al., 1983, 1990), it is consistent with those in which P3 was elicited in a complex task and that reported no P3 latency–IQ relationship. In an n-back task no association was found between P3 latency and WAIS-R (Gevins and Smith, 2000), in both a 2-CRT and 5-CRT task there was no relationship between P3 latency and working memory span (Nittono et al., 1999), and in a Sternberg memory task P3 latency to the probe, although increasing with set size along with response time which correlated with IQ, did not correlate with IQ (Houlihan et al., 1998).

In contrast to latency, the weak association found between parietal P3 amplitude and task performance indicates only a tendency for those who performed the task better to allocate more resources for processing. One explanation for this may be that the relationship between P3 amplitude and performance is subject to the differential employment of strategies, as suggested in some studies (Fabiani et al., 1986; Karis et al., 1984), with differences in the degree of involvement affecting P3 amplitude and concealing the association with task performance. For example, some individuals in order to perform relatively well on the task may allocate more processing resources, indexed by a larger P3 amplitude, to compensate for their smaller working memory capacity. Indeed, imaging studies have found that for a given level of performance there is differential activation of the dorsolateral prefrontal cortex, with the more difficulty an individual has in producing the correct response the more activation of the prefrontal cortex required, with greater activation reflecting individual differences in processing efficiency (Rypma and D'Esposito, 1999). There is also evidence that high-ability individuals develop strategies that make relatively greater use of parietal regions, whereas low-ability subjects rely more on frontal regions (Gevins and Smith, 2000). Thus, with a task imposing a higher load on working memory capacity we might expect individual differences in P3 amplitude and task performance to be more similarly pronounced, and for a stronger relationship between P3 amplitude and task performance to emerge. In line with this is the finding of an association between working memory span and P3 amplitude elicited in the more difficult 5-CRT but not in the easier 2-CRT task (Nittono et al., 1999). Similarly, in the low demanding oddball task P3 amplitude has not been associated with cognitive ability (Howard and Polich, 1985; O'Donnell et al., 1992; Polich and Martin, 1992; Polich et al., 1990) whereas in the more complex n-back task P3 amplitude was found to be associated with reaction time (Gevins and Smith, 2000). To the contrary, greater perceptual demands to the memory set in a Sternberg task did not lead to a clear relation between P3 amplitude and cognitive ability (Houlihan et al., 1998).

Given the finding of a weak phenotypic association between P3 amplitude and task performance it was not surprising that there was only a small overlap between genetic influences on P3 amplitude and task performance. The low genetic

association suggests that genes influencing the allocation of resources for encoding the target stimulus may be independent of the genes influencing task performance, or at least under the cognitive demands imposed by the delayed-response task in this study. This is in contrast to the findings discussed above for P3 latency that mediated 22% of the total genetic variation in task performance. There was also no indication that genes mediating P3 amplitude influenced any variability in IQ. However, the finding of a genetic influence on P3 amplitude independent of that on IQ has been demonstrated previously (Katsanis et al., 1997). One possible explanation, given the finding of a substantial overlap in the genetic influence on baseline EEG and P3 amplitude, at least in males (Anokhin et al., 2001), is that the genetic variation in P3 amplitude in the present study is largely mediated by genes influencing EEG spectral power. Although there is some evidence that there is a difference in EEG alpha power between highly gifted individuals and those in the normal range (Alexander et al., 1996), it is not yet known what the relationship is between EEG power and cognitive ability.

In summary, our exploration of the genetic sources of covariation among psychophysiological, performance and psychometric indices of cognition demonstrated that while a faster P3 latency was associated with better task performance, with genes accounting for a large part of the covariation, genetic influences on P3 amplitude were largely independent of behavioral performance. Although a common genetic factor influenced the relationship between task performance and IQ, individual differences in P3 latency and P3 amplitude that were significantly influenced by genes were not sensitive to individual differences in IQ. The findings may be task specific, and future studies at the phenotypic level may help gain a better understanding of the conditions under which the amplitude and latency of the P3 component of the ERP is sensitive to individual differences in task performance and IQ, by using tasks with varying cognitive demands, and by examining whether the same associations can be found in those of low and high ability. At the genetic level, it would be appropriate to expand the current analyses to include other endophenotypes. For example, baseline EEG, inspection time, or working memory span, to find out whether the genes influencing these cognitive indices share some underlying target process with the amplitude or latency of the P3 which may be independent or in common with measures of general cognitive ability.

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