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Genetic Mediation of the Correlation Between Peripheral Nerve Conduction Velocity and IQ

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Variation in peripheral nerve conduction velocity (PNCV) and intelligence was studied in 18-year-old Dutch twins. It has been suggested that both brain nerve conduction velocity and PNCV are positively correlated with intelligence (Reed, 1984) and that heritable differences in nerve conduction velocity may explain part of the well-established heritability of intelligence. The relationship among IQ, obtained with the Wechsler Adult Intelligence Scale, and median nerve PNCV was examined in 159 twin pairs. Genetic analyses showed a heritability of 81% for IQ and 66% for onset PNCV. The small but significant phenotypic correlation between IQ and onset PNCV (.15) was entirely mediated by common genetic factors. Analyses of difference scores for PNCV of this study and PNCV from the same subjects collected at age 16 suggest that there might still be development in PNCV in this age interval. This maturation is highly controlled by genetic factors. It is suggested that variation in IQ that is associated with nerve conduction velocity becomes apparent only after the developmental processes in peripheral nerves are completed. This is in line with the suggestion of increasing heritability of IQ in adulthood.

KEY WORDS: Median nerve; twins; intelligence; maturation; heritability.

INTRODUCTION

The strong heritability for psychometric intelligence is well established. Twin and family data support the existence of genetic influences upon human cognitive abilities. Approximately 50–60% of the phenotypic variance in adult IQ is associated with genetic differences among individuals (Bouchard and McGue, 1981; Plomin and Rende, 1991; Boomsma, 1993; Bouchard, 1993). Since genetic polymorphisms code for biological differences, these findings give strong evidence for the existence of biological determinants of intelligence differences between individuals. This biological intelligence is influenced by genes which code for neurophysiological and biochemical factors and processes in the brain but can also be modified by environmental factors. Despite the considerable practical applications of psychometric IQ, it remains an uncertain mixture of capacity and acquired knowledge, and a more complete understanding of the nature of human intelligence should include knowledge of biological intelligence (Eysenck, 1993).

Among a great number of biological variables, peripheral and central nerve conduction velocities have been investigated as potential biological determinants of intelligence. Nerve conduction velocity (NCV) reflects the speed with which electrical impulses are transmitted along nerve fibres and across synapses. Reed (1984) hypothesized that the heritability of IQ may be a result of genetic variability in the structure and amount of "transmission proteins" which set limits on information processing rates and on intelligence. Transmission

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Table I. Studies on the Relationship Between Peripheral Nerve Conduction Velocity and IQ[a]

	Correlation, IQ–PNCV	Segment median nerve	Mean PNCV (m/s)	IQ test	Temperature control	Age range (mean age)	Number of subjects
Vernon & Mori (1992)	.41*[b]	Wrist–fingers Wrist–elbow Elbow–axilla	63.9	MAB	Experimentally	18–42 (24)	85
Vernon & Mori (1992)	.46*	Wrist–fingers	60.1	MAB	Experimentally	18–38 (23)	88
Barret *et al.* (1990)	−.00[c]	Fingers–wrist	39.7	RAPM	Experimentally	18–41 (25.6)	44
Reed & Jensen (1991)	.04[d] −.07	Wrist–elbow	68.9 67.1	RSPM & RAPM	Statistically	18–25 (20.3)	200 (males)
Wickett & Vernon (1994)	.02[e] −.12	Wrist–elbow Wrist–fingers	60.5 59.0	MAB	Experimentally	20–30 (24.6)	38 (females)
Rijsdijk *et al.* (1995)	−.02	Wrist–elbow	63.7	RSPM	Experimentally	14.8–18 (16.1)	312
This study	.15*	Wrist–elbow	59.5	WAIS	Experimentally	16.4–19.5 (17.6)	346

[a] RSPM, Raven Standard Progressive Matrices; RAPM, Raven Advanced Progressive Matrices; MAB, Multidimensional Aptitude Battery; WAIS, Wechsler Adult Intelligence Scale.
[b] Eight PNCV measures of these segments were aggregated into a single one, GNCV. The correlation between GNCV and IQ is reported.
[c] Mean correlation of four PNCV measures with IQ.
[d] Correlations of two samples: community college (RSPM) and university students (RAMP).
[e] Correlations with PNCV of two segments.
* Significant correlation.

proteins include enzymes involved in myelin sheathing and neurotransmitters (which are synthesised by specific enzymes). Genetic variability in the structure and amount of transmission proteins may determine information processing rates. Reed (1988) suggested that peripheral nerve conduction velocity (PNCV) as a quantitative genetic trait may model central nerve conduction velocity. PNCV is a relatively easy obtainable measure of nerve conduction speed. In humans, it is a well-established, extensively studied neurological trait, used for diagnostic purposes in neuromuscular and neurological diseases (Desmedt, 1980; Ma and Liveson, 1983; Oh, 1993). The genetic background of PNCV variation was first studied in mice populations by Hegmann *et al.* (1973), who observed low to median heritabilities in tail NCV (narrow-sense heritabilities of .1 to .2; broad-sense heritabilities of .2 to .3). Reed (1988) also found heritabilities of .23 ± .05 for tail NCV in mice. In humans, the genetic architecture of PNCV was studied in twins (Rijsdijk *et al.*, 1995) and was, as predicted by Reed (1988), a substantially heritable trait. The heritability for median nerve conduction velocity, computed for onset latencies of orthodromically assessed compound mixed nerve action potentials, was 76%. Variation in PNCV has been studied in relation to individual differences in intelligence.

Table I provides an overview of the results of studies conducted on peripheral NCV and IQ. Vernon and Mori (1992) reported correlations between PNCV in the median nerve and IQ score on the MAB [Multidimensional Aptitude Battery (Jackson, 1984)] in two independent samples of Canadian university students: .43 (n = 85) and 46 (n = 88). They concluded that a general factor of neural efficiency is a major aspect of psychometric IQ. However, Barrett *et al.* (1990) found no correlation between median NCV and Raven Advanced Progressive Matrices in 44 British adults. Wickett and Vernon (1994) also failed to replicate the findings of the earlier studies of Vernon and Mori (1992), submitting the same IQ test and PNCV procedure to a smaller sample of 38 females (20 to 30 years of age). Reanalyses of the data of 1992 yielded sex difference in the relationship be-

tween NCV and IQ, with a pronounced correlation in males. Wickett and Vernon (1994) speculated that males may rely more heavily on neural speed to perform cognitive tasks, whereas for females other neural processes might play the predominant role.

In addition to these studies of peripheral NCV and IQ, two other studies investigated the relation among peripheral NCV, central NCV, and IQ simultaneously. Reed and Jensen (1991) divided latencies of visual evoked potentials (VEP) by head length to obtain an indicator of central NCV. The latency of a VEP reflects the speed of conduction along the primary visual pathway (retina–thalamus, v1). Reed and Jensen found no correlation between visual pathway NCV and IQ [though an earlier report (1989) from the same project gave correlations of .27 and .37 between visual pathway NCV and IQ]. There was no correlation between peripheral NCV and the visual pathway NCV or between peripheral NCV and IQ (n = 200).

Reed and Jensen (1993) also studied the relation among central NCV, peripheral NCV, and IQ by means of somatosensory evoked potentials (SEPs). SEPs are electrical signals recorded from the scalp over the relevant part of the somatosensory cerebral cortex following stimulation of some peripheral nerve. Three SEPs are usually observed following one single stimulation of the median nerve at the wrist. N13 is generated in the region of the cervical spinal cord, N19 is generated in the thalamus, and P22 is generated in the somatosensory cortex. The latency of the N13 represents peripheral conduction time. The latency difference P22 − N19 represents the thalamus–parietal cortex transmission time and reflects brain conduction time. The P22 − P19 latency difference correlated negatively with IQ (−.22). Peripheral latency (wrist to cervical spinal cord) did not correlate with IQ. This finding was in agreement with the previous study of the same population (Reed and Jensen, 1991), where no correlations were found between median nerve NCV and IQ. Inadequate temperature control in both studies (statistically instead of physically) should be considered when evaluating these findings, as temperature is regarded as the most important source of error that can affect the assessment of peripheral NCV (e.g., Kimura, 1984; Rivner *et al.*, 1990; Oh, 1993; Letz and Gerr, 1994). Reed and Jensen did not report on the correlation between peripheral and central tract latencies, nor did they report on velocity measures for the peripheral and central tracts.

Several studies have examined the relation between other measures of central conduction speed and IQ. A rational for these investigations is given by the myelin hypothesis (Miller, 1994), which postulates that higher intelligence is associated with larger brain size. Positive correlations between brain size and intelligence have been found in studies using magnetic resonance imaging (e.g., Wickett *et al.*, 1994; Willerman *et al.*, 1991; Raz *et al.*, 1993, Schultz *et al.*, 1993). Miller proposed that thicker myelin sheaths could be the major explanation for the positive correlation between brain size and IQ. Thicker myelin sheathed nerves are faster, prevent accidental signaling in adjacent neurons and therefore are associated with faster information processing speed and higher intelligence (Miller, 1994).

Clearly, there are studies which found a significant relationship between peripheral NCV and IQ and between central NCV and IQ, but in the studies that investigated the three measures simultaneously, there was no evidence that peripheral NCV was correlated with central NCV. However, besides experimental artifacts such as temperature control, the absence of a peripheral-to-central NCV correlation may be real. There are differences in peripheral and central nervous system properties that should be considered. Myelin, the membrane characteristic of nervous tissue that is responsible for transmission velocity, is formatted and maintained by oligodendrocytes in the central nervous system. In the peripheral nervous system the Schwann cells are the myelin-forming cells. These cells differ in a number of ways, e.g., in the manner of controlling the formation of myelin, in the coding for production of myelin, in their origin, and in their biochemics and structure. A single oligodendrocyte maintains as many as 30–50 internodes of myelin. In contrast, a single Schwann cell envelopes just one internode (Kandel *et al.*, 1991). The genes in Schwann cells that encode myelin are turned on by the presence of axons, whereas expression of the genes in oligodendrocytes that encode for central myelin depends on the presence of astrocytes, the other major glial cell type in the central nervous system (Kandel *et al.*, 1991). Oligodendrocytes originate from precursor cells in the ventricle zone of the neural tube, whereas Schwann cells are derived from migrating neural crest cells

(e.g., Jacobson, 1991). Given these differences, peripheral and central neurophysiological processes might not be fully comparable. However, there are a number of clinical studies providing evidence that diseases of and inflictions upon the nervous system show negative effects on both peripheral and central conduction. Clinical NCV studies in, for example, lead-, zinc-, and copper-exposed workers (Araki *et al.*, 1987), in patients with primary hypothyroidism (a hormone dysfunction) (Abbott *et al.*, 1983), and in HIV-1 patients (Pinto *et al.*, 1992) show slowing in both peripheral and central NCV when patients are compared with controls, even though there was no clinical evidence of neurological impairment.

Inspired by the original findings of Vernon and Mori, we designed a study to investigate the relationship between PNCV and intelligence longitudinally in a sample of Dutch twins. We investigated to what extent the variation in IQ is attributed to variation in PNCV and to what extent the PNCV-IQ covariation is mediated by genetic and/or environmental factors. At the first test occasion at age 16, no correlation was found between scores on the Raven Standard Progressive Matrices (Raven, 1958) and PNCV measured in the median nerve (Rijsdijk *et al.*, 1995). This paper reports the correlation between PNCV in the median nerve and intelligence, determined by the Wechsler Adult Intelligence Scale (WAIS) in the same twin pairs at age 18. Using the WAIS IQ test was suggested to increase the probability of replicating the findings of Vernon and Mori, because the WAIS is highly correlated with the MAB [r = .91 for full-scale IQ (Jackson, 1984)]. This is in contrast with the Raven Advanced Progressive Matrices, which has a common variance of only 50% with the WAIS full-scale IQ [r = .72 (Vernon, 1983)]. In our sample the common variance between the Raven Standard Progressive Matrices and the WAIS full-scale IQ was even lower: 44% (r = .66). We also looked at the stability of the correlations between PNCV measured at age 16 and PNCV at age 18.

SUBJECTS AND METHODS

Subjects. This PNCV study was part of a longitudinal project in which genetic and environmental influences on brain development were examined (van Beijsterveldt *et al.*, 1995, 1996). At age 16, 213 twin pairs participated in the study; at age 18, 196 pairs came back for a second time. The 17 twin pairs who dropped out did not differ significantly in IQ score compared to the others. PNCV and IQ data presented in this paper were collected at the second visit of the twins to the laboratory. Mean age (17.6; SD = .54) was equal for males and females. Subjects also participated in a large questionnaire study on health, personality and lifestyle factors such as smoking and sports participation (Koopmans *et al.*, 1994).

For 117 twin pairs zygosity was determined by blood and DNA typing, and for the others by questionnaire data concerning physical similarity and the frequency at which the twins get confused by family members and strangers. For the blood- and DNA-typed group questionnaire data were available for 85 pairs. The percentage correctly classified zygosities based on the questionnaire information compared with blood-group polymorphism and DNA was 95%.

IQ data were available for 37 MZM, 31 DZM, 46 MZF, 36 DZF, and 44 DOS twin pairs. Data for median NCV were available for a subgroup of 34 MZM, 22 DZM, 40 MZF, 27 DZF, and 36 DOS complete pairs. For another 28 twin pairs, PNCV data were available for only one twin of a pair (15 males and 13 females). In the bivariate genetic analysis and the analyses of the phenotypic correlations between PNCV and IQ, data from these incomplete pairs were included. Missing PNCV data for one or both twins in a pair were due to technical and procedural problems (e.g., difficulty in palpation of the nerve and ambiguous latency readings).

Intelligence Test. The Dutch translation of the Wechsler Intelligence Scale (WAIS) was administered (Stinissen *et al.*, 1970).

Physical Exercise. Questionnaire data on sports participation and other physical activities (e.g., cycling as transportation means) were available for 163 twin pairs and examined in relation to peripheral NCV. Physical activity level was proposed to be a covariate for peripheral NCV that should be controlled for when examining the relationship between PNCV and IQ (Reed, 1993).

Nerve Conduction Velocity. PNCVs were determined for the wrist–elbow segment of the median nerve of the right arm. The median nerve is a mixed motor and sensory nerve. Supramaximal stimulation was used, i.e., stimulation of the nerve at a current value beyond which the amplitude of the nerve action potential no longer increases. From

each subject two compound nerve action potentials (CNAP) were obtained; each CNAP was signal-averaged over eight nerve stimulations. For each CNAP three components were distinguished: onset, peak, and end latency. Reliability for PNCV measures was obtained by correlating the latencies of the two CNAPs. For the phenotypic correlations and the genetic analyses the two onset, peak, and end latencies were averaged. The distance between the active stimulating and the recording electrodes (wrist–elbow distance in millimeters) was divided by the mean onset, peak, and end latencies (milliseconds), yielding one onset, peak, and end nerve conduction velocity measure per subject.

Onset and peak PNCV reflect the conduction in the fast-conducting (large-diameter) nerve axons and the average-conducting (average diameter) nerve axons, respectively, while end PNCV involves slow-conducting (small diameter) axons (Ma and Liveson, 1983; Oh, 1993). Onset PNCV is commonly used in studies examining the relation between IQ and PNCV, because it reflects conduction of the fast nerve fibers.

Two important errors can bias nerve conduction velocity assessment: latency readings and errors in surface measurement of the length of the nerve (Oh, 1993). To correct for the first type of error, compound nerve action potentials with ambiguous onset latencies were excluded from the sample. Temperature was experimentally controlled and kept at a constant level (33°C). For a detailed description of the action potential acquisition apparatus, procedure, and PNCV computation, see Rijsdijk *et al.* (1995).

Statistical Analyses. The effect of sex on mean IQ and PNCV measures was assessed by likelihood-ratio χ^2 tests using the computer program LISREL VII (Jöreskög and Sörbom, 1988). These tests compare the fit of a model that constrained parameter estimates for mean IQ and PNCVs to be equal across sexes to one which allowed them to vary in males and females, while taking into account the dependency that exists between observations from twins (Boomsma *et al.*, 1993). Phenotypic correlations among PNCV, IQ, and age were estimated using LISREL VII. To the variance–covariance matrices of the five sex × zygosity groups and the two singleton groups, a model was fitted in which correlations as well as standard deviations were estimated. Sex and zygosity differences in correlations were tested by comparing the fit of models which constrain correlations to be equal across groups with models in which correlations are set free. Significance of correlations was tested by comparing the fit with models in which correlations are constrained at zero.

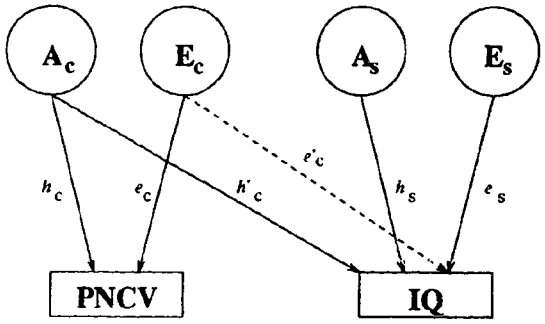

Fig. 1. Bivariate genetic model for PNCV and IQ. A_c and E_c reflect the genetic and environmental influences common to PNCV and IQ; A_s and E_s reflect the genetic and environmental influences specific for IQ.

Genetic Analyses. Quantitative genetic model fitting was carried out on variance–covariance matrices to decompose the phenotypic variance. Sources of phenotypic variation considered were A, additive genetic variation (i.e., the sum of the average effects of the individual alleles at all loci); D, dominance genetic variation; and E, a random environmental deviation that is not shared by family members. Dominance genetic effects, rather than C (common or shared environmental variation), were considered, because of the high MZ-versus-DZ twin correlations. This model assumes negligible effects of assortative mating and genotype–environment correlation and/or interaction. Relative contributions of the genetic and environmental influences to observed individual differences were estimated by maximum likelihood, using the computer program Mx (Neale, 1995). Also, 80% confidence intervals for the heritability estimates were computed (Neale and Miller, 1996). Goodness of fit was assessed by likelihood-ratio χ^2 tests.

Bivariate genetic analysis was used for modeling the relationship between PNCV and IQ. Two sets of latent A, D, and E factors were specified: common factors influencing both PNCV and IQ and specific factors influencing IQ only. Figure 1 shows the model for one member of a twin pair, where A_c and E_c are the genetic and environmental

Table II. Estimates of Means and Standard Deviations for WAIS IQ Scores and Peripheral Nerve Conduction Velocity Measures[a]

	Males		Females		Sex Differences, $\Delta\chi^2$ (df = 1)
	M	SD	M	SD	
WAIS VIQ	110.2	12.5	109.7	11.7	0.14
WAIS PIQ	115.9	11.9	116.8	11.7	0.35
WAIS FSIQ	113.7	11.7	113.9	11.7	0.01
Onset PNCV (m/s)	59.3	3.3	59.9	3.6	3.34
Peak PNCV (m/s)	50.3	2.8	49.9	2.8	0.90
End PNCV (m/s)	43.2	2.4	41.8	2.3	21.03*

[a] WAIS, Wechsler Adult Intelligence Scale; VIQ, Verbal IQ; PIQ, Performal IQ; FSIQ, Full Scale IQ; PNCV, peripheral nerve conduction velocity. Estimates for 163 males and 183 females.

* $\Delta\chi^2$ (df = 1) > 3.84 and implies a significant difference between males and females.

influences common to PNCV and IQ, and A_s and E_s are the genetic and environmental influences specific to IQ. The effects of A_c and E_c on PNCV are represented by the parameters h_c and e_c, and the effects of A_c and E_c on IQ by the parameters h'_c and e'_c.

RESULTS I

Raw score distributions of the WAIS full-scale IQ and onset PNCV showed acceptable symmetry (skewness, −.3 and .002; kurtosis, −.42 and −.21, respectively), as did the distributions of WAIS verbal IQ (VIQ), WAIS performance IQ (PIQ), peak PNCV, and end PNCV.

In Table II the means and standard deviations for WAIS full-scale IQ, VIQ, PIQ, and PNCV measures are presented. The onset PNCV mean of 59.6 m/s (SD = 3.4) for the total sample (n = 346) agrees with values reported in the literature for adults (age range, 20–60; temperature, above 31°C): 55.99 ± 3.3 (Oh, 1993). The observed mean WAIS full-scale IQ of 113.6 was higher and the standard deviation of 11.2 was lower than the population mean and standard deviation (X = 100, SD = 15). In a recent validation study (n = 601) of four subtests of the Dutch translation of the WAIS (Mulder *et al.*, 1995), it appeared that scores on all four tests were higher than scores of the Dutch normative sample (Stinissen *et al.*, 1970). Bouma *et al.* (1996) suggested that this observation might be a consequence of increasing population IQ and that WAIS IQ scores based on the 1970 norms might be somewhat overestimated. There were no differences between males and females in mean scores for IQ or for onset and peak PNCV. Mean end PNCV showed a significant sex difference [$\chi^2(1)$ = 26.1]. Reliabilities for the PNCV measures obtained by the correlations for onset, peak, and end latency between the two initial CNAPs available for every subject were .97, .98, and .98, respectively.

Table III. Maximum-Likelihood Estimates of the Phenotypic Correlations Between Peripheral Nerve Conduction Velocity and WAIS-IQ[a]

	WAIS-FSIQ	WAIS-VIQ	WAIS-PIQ
Onset PNCV	.15	.15	.15
Peak PNCV	.16	.17	.14
End PNCV	.18	.14	.15

[a] WAIS, Wechsler Adult Intelligence Scale; FSIQ, Full Scale IQ; VIQ, Verbal IQ; PIQ, Performal IQ; PNCV, peripheral nerve conduction velocity. All correlations are significant.

Potential confounders of PNCV are age, height, temperature, (Oh, 1993; Ma and Liveson, 1983; Rivner *et al.*, 1990; Stetson *et al.*, 1992), and physical exercise status (Reed, 1993). Age, height, and physical exercise status, based on sports activity and daily cycling exercise, did not show a correlation with PNCV. Arm temperature was experimentally controlled for and showed no correlation with PNCV. Table III shows the maximum-likelihood estimates of the phenotypic correlations between the PNCV measures and the IQ scores. All PNCV–IQ correlations could be equated across twins, zygosity, and sex without worsening of fit. All PNCV–IQ correlations were significant.

The twin correlations for the IQ scores and the PNCV measures are given in Table IV, showing higher MZ than DZ correlations for all measures. The pattern of the female twin correlations (high MZ versus low DZ correlations) for WAIS VIQ, peak PNCV, and end PNCV suggest dominance genetic effects. Therefore, a univariate *ADE* model for females and *AE* model for males was tested against the *ADE* sex-differences model. For all three variables the dominance structure could be dropped without worsening of fit and the reduced *AE* no-sex-difference model gave the best explanation of the data. For onset PNCV it was the correlation pattern for males that suggested a dominance genetic structure to be involved. This

dominance structure could be omitted and further reduction of the model also showed the no-sex-difference *AE* model to have the best fit. The correlation pattern for WAIS full-scale IQ and WAIS PIQ suggested dominance genetic influences for both males and females, but the reduced *AE* no-sex-difference model again showed the best fit to the data. Table V gives the univariate estimates and heritabilities for PNCV and IQ measures for the subsample with both PNCV and IQ data (159 pairs). Likelihood-based confidence intervals (CI) provide information about the precision of the estimates (Neale and Miller, 1996). In Table V the 80% CIs for the heritability estimates for all variables are reported. Nonoverlapping intervals, which is the case, e.g., for WAIS verbal IQ and WAIS performance IQ, indicate that heritabilities are significantly different. The heritability for WAIS full-scale IQ was 81%, and for onset PNCV the heritability was 66%. WAIS IQ data were available for a larger group (194 pairs). The heritability for WAIS full-scale IQ for this sample was 82% (Rijsdijk and Boomsma, 1996).

Onset PNCV and the WAIS full-scale IQ score were used to investigate the PNCV–IQ relationship, using the genetic model presented in Fig. 1. In Table VI the bivariate analysis results are presented. An *ADE* model with sex differences did not show a better fit than a model in which the parameters were equated among males and females. In the next step the common dominance genetic factor could be omitted without worsening of fit. In the reduced *AE* no-sex-difference model the common unique environmental influences of PNCV on IQ (e'_c) could be fixed at zero without deterioration in fit [$\Delta\chi^2(1) = .22$, $p = .64$], whereas the common genetic influences (h'_c) could not be constrained at zero [$\Delta\chi^2(1) = 4.15$, $p = .04$]. These results indicate that all common variance in PNCV and IQ can be explained by common additive genetic factors ($\chi^2_{51} = 58.4$, $p = .22$). This model gave a good fit to the data. Thus, the PNCV–IQ relationship is based purely on common genetic mediation. The genetic correlation (r_g) between PNCV and IQ as estimated by Mx was .20. The heritability for onset PNCV was .66, with an 80% CI of .58–.73. Heritability for WAIS full-scale IQ score was .81, with a 80% CI of .75–.84. The phenotypic correlation between onset PNCV and WAIS full-scale IQ based on the Mx estimates was .15. In Table VII the parameter estimates of specific and common genetic and environmental influences for the best fitting model are presented.

Table IV. Twin Correlations for PNCV Measures and WAIS IQ Scores[a]

	Onset PNCV	Peak PNCV	End PNCV	WAIS VIQ	WAIS PIQ	WAIS FSIQ
MZM (n = 34)	.80	.78	.79	.88	.74	.86
DZM (n = 22)	.21	.41	.52	.47	.30	.37
MZF (n = 40)	.63	.71	.71	.85	.65	.82
DZF (n = 27)	.31	.19	.10	.30	.24	.34
DOS (n = 36)	.39	.52	.45	.24	.20	.19

[a] PNCV, peripheral nerve conduction velocity; WAIS, Wechsler Adult Intelligence Scale; VIQ, verbal IQ; PIQ, performal IQ; FSIQ, Full-Scale IQ. n = number of pairs with both PNCV and IQ data.

Table V. Univariate Estimates of Genetic (a) and Environmental (e) Path Coefficients and Heritabilities with 80% Confidence Intervals for PNCV and IQ Measures[a]

	χ^2 (df = 13)	p	a	e	h^2 (%)	80% CI for h^2 (%)
Onset PNCV	15.08	.30	2.72	1.94	66	58–73
Peak PNCV	14.04	.37	2.31	1.46	71	64–77
End PNCV	13.88	.38	1.95	1.22	72	65–78
WAIS-VIQ	13.72	.44	10.95	5.02	83	78–86
WAIS-PIQ	3.62	.99	9.43	6.60	67	59–74
WAIS-FSIQ	10.18	.68	10.46	5.08	81	76–85

[a] PNCV, peripheral nerve conduction velocity; WAIS, Wechsler Adult Intelligence Scale; VIQ, Verbal IQ; PIQ, Performal IQ; FSIQ, WAIS Full-Scale IQ. Best-fitting model for all variables: *AE* no-sex-difference model.

Table VI. Bivariate Model-Fitting Results for Onset Nerve Conduction Velocity with WAIS Full-Scale IQ[a]

Model	χ^2	df	p
ADE with sex diff.	48.73	38	.11
ADE, no sex diff.	56.13	47	.17
AE, no sex diff.	58.26	50	.19
AE, no sex diff. and no e'_c[b]	58.40	51	.22
AE, no sex diff. and no h'_c	62.41	51	.13

[a] e'_c, environmental path from PNCV to IQ; h'_c, additive genetic path from PNCV to IQ.

[b] Best-fitting model: *AE*, no sex differences and no common environmental influences.

Table VII. Genetic- and Environmental-Specific and Common Effects of the Bivariate Model of PNCV and IQ[a]

Genetic & environmental-specific effects for IQ		Genetic & environmental common effects for IQ		Genetic & environmental common effects for PNCV	
h_s	e_s	h'_c	e'_c	h_c	e_c
10.121	5.121	2.054	0.00	2.718	1.960

[a] h_c and e_c are the components of the common genetic and environmental factors influencing PNCV; h'_c is the component of the common genetic structure, reflecting the genetic mediation of the correlation between PNCV and IQ; $e'_c = 0$ means no environmental correlation between PNCV and IQ; h_s and e_s are the components of the genetic and environmental specific factors exclusively influencing IQ.

DISCUSSION I

For WAIS full-scale IQ a heritability estimate of 81% was observed. This is in line with or somewhat higher than most family and twin studies. As Reed (1988) predicted, human peripheral NCV was found to be a substantial heritable trait (66%). Reed suggested that PNCV, as a heritable trait, to some extent could explain part of the genetic variation in human intelligence, and consequently the PNCV-IQ relationship should be mediated by genetic factors. A low but significant correlation between peripheral NCV and IQ was found in our sample, and this correlation was mediated solely by common genetic factors. The genetic correlation between onset PNCV and IQ was .20.

Peripheral NCV, measured in the same subjects at age 16, showed a heritability of 76%. No correlation was found between Raven Standard Progressive Matrices IQ scores and peripheral NCV. The lack of correlation between IQ and peripheral NCV was also found in other studies using the Raven test (Reed and Jensen, 1991; Barrett *et al.*, 1990). The use of the Raven IQ test was proposed as a possible explanation for the lack of correlation between PNCV and IQ, because the correlations of .43 and .46 between PNCV and IQ found by Vernon and Mori were obtained using the Multi Aptitude Battery (MAB). The WAIS IQ test was used in the present study to enlarge the probability of replicating the results of Vernon and Mori (1992), though Wicket and Vernon (1994) failed to replicate a significant correlation between the MAB IQ scores and PNCV in a sample of adult females. However, the correlation of the Raven IQ scores of our first study with PNCVs in the second study (.17; $p < .05$) was higher then the correlation between WAIS full-scale IQ and PNCVs in the second study, suggesting that lack of correlation was not due to the Raven IQ test.

Results for both test occasions revealed the peripheral NCV measure to be a substantial heritable trait, 76 and 66%, respectively. However, the test–retest correlations of the PNCV measures were very low: for onset PNCV, .13 ($p < .05$); for peak PNCV, .08 (ns); and for end PNCV, .20 ($p < .05$). PNCV data at both age 16 and age 18 were available for 293 individuals. No changes were made in acquisition procedure, apparatus, experimenter, and nerve conduction velocity computation. Possible statistical artifacts, such as nonnormality, that might explain this lack of correlation were extensively tested by means of randomization tests. Randomization tests do not imply assumptions about binormality, and the significance (p value) of a statistical test is derived from the empirical distribution of p values based on (part of) all possible combinations. When results of a randomization test of, e.g., test–retest correlation are similar to the probability value of the classical test, the possibility of a wrong decision based on the classical test, when a nonbinormal distribution leads to a distorted p value, is ruled out. No differences in the probability values for the test–retest correlations of latencies, wrist–elbow distance, and PNCVs were obtained in either way. These results imply that lack of stability in the PNCV data is not caused by statistical artifacts as nonbinormality and justify the use of parametrical tests. The twin correlation pattern, especially the high MZ correlations, also suggests that the lack of test–retest correlation, is not due solely to measurement errors and technical pitfalls. Moreover, the low DZ PNCV twin correlations relative to MZ correlations suggest that high MZ twin correlations are not the result of correlated measurement errors. Additional evidence for PNCV measurement consistency or reliability can be obtained by split-half correlations for the three latencies between the two initial compound nerve action potentials available for every subject. Reliability for onset, peak, and end latency was .97, .98, and .98, respectively. The same reliability indices were observed for the three latencies of the first test occasion: .97, .99, and .99, respectively.

We speculate that the lack of correlation between age 16 and age 18 might be explained by

ongoing maturation processes in this age range. Nerve conduction velocity increases in a logarithmic function. From birth to approximately age 4–6, peripheral NCV increases rapidly as a result of the myelination process and the increase in the number of large axonal fibers (Cruz Martinez *et al.*, 1978; Wagner and Buchthal, 1972; Gamstorp and Shelburne, 1965). The existence of double peaks in the sensory nerve action potential (up to age 6) indicates the presence of two groups of fibers with different degrees of maturation. No further increase in PNCV is noted between 4–6 and 16 years of age. PNCV decreases in the late twenties. The rate of decrease for mixed PNCV per decade is approximately 4 m/s in the median nerve (Oh, 1993).

It is reasonable to assume that, with respect to PNCV development, individual growth curves show the same morphology but have different slopes, e.g., the speed of maturation might differ per individual. It is also reasonable to assume that maturation processes might be more alike in MZ twins compared to DZ twins.

We, therefore, decided to examine whether ongoing maturation processes in this age sample might explain our findings of (1) a significant correlation of PNCV with both Raven and WAIS IQ at age 18 but not at age 16, (2) a low test–retest correlation between PNCV assessed at age 16 and that at age 18, and (3) high MZ correlations (and high heritabilities) at both age 16 and age 18. A genetic analysis of PNCV difference scores (PNCV assessed at test occasion II − PNCV assessed at test occasion I) was carried out. Then the relation of PNCV and IQ was studied in subjects who showed positive and negative difference scores. Positive difference scores might indicate that PNCV has not yet reached the highest value and negative difference scores might reflect a phase in which this value was reached and PNCV is then declining. It is possible that the PNCV–IQ relation is fully observable only once the PNCV has reached its highest value.

RESULTS II

To study the maturation hypothesis a difference score between onset nerve conduction velocity at the second and that at the first test occasion was calculated (difONCV). DifONCV was normally distributed ($X = -3.7$, SD = 8.1; skewness = −.16; kurtosis = −.23), with about 70% of the observations between one standard deviation from the mean (Fig. 2). The difference scores for peak PNCV (difPNCV) and end PNCV (difENCV) were also normally distributed (skewness = −.02 and .00 and kurtosis = .15 and .5, respectively). In subjects with positive difference scores, PNCV is still increasing from age 16 to 18. In subjects with negative difference scores, PNCV has supposedly reached the highest value and is decreasing. The latter group is in a relatively stable maturation phase or in a phase representing PNCV decrease. There were sex differences for mean difONCV and mean end PNCV difference score (difENCV). Mean difONCV was −1.5 for males and −4.3 for females [$\chi^2(1) = 7.2$]. Mean difENCV was 4.3 for males and 2.9 for females [$\chi^2(1) = 5.9$]. There was no sex difference in mean peak difference score [1.1; $\chi^2(1) = 3.2$]. No significant age differences were seen between the groups with positive and those with negative difference scores.

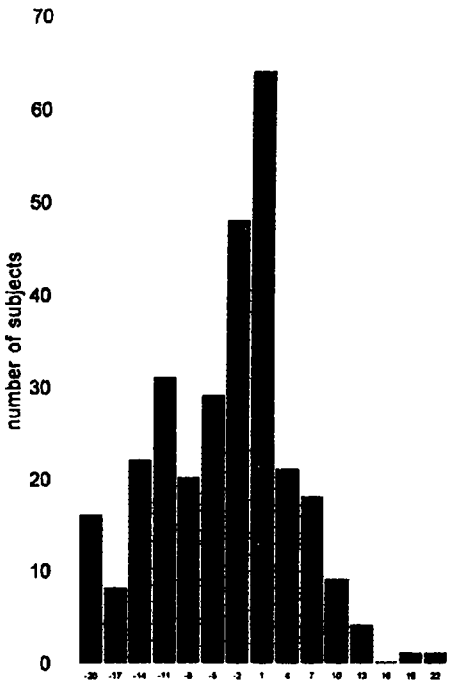

Fig. 2. Distribution of the difference scores for onset PNCV between age 18 and age 16 (difONCV). On the X axis are the difONCV scores.

The twin correlations for difONCV suggest genetic determination (Table VIII). The higher MZ

Table VIII. Twin Correlations and Heritabilities with 80% Confidence Intervals for PNCV Difference Scores[a]

	MZM (n = 22)	DZM (n = 15)	MZF (n = 33)	DZF (n = 21)	DOS (n = 29)	h^2_{males} (%)	80% CI for h^2 (%)	$h^2_{females}$ (%)	80% CI for h^2 (%)	χ^2 (df = 10)
difONCV	.85	.12	.83	.38	.01	86	78–91	87	81–91	8.13
difPNCV	.85	.13	.69	.39	.05	84	75–89	73	61–81	9.64
difENCV	.78	.05	.73	.35	−.22	75	61–84	74	62–82	12.65

[a] difONCV, difPNCV, and difENCV—difference scores between onset, peak, and end PNCV measured at age 18 and at age 16. Best-fitting model for all variables was *ADE* for males and *AE* for females. n = number of twin pairs.

compared to DZ twin correlations suggested dominance genetic effects. In contrast to the PNCV measure, the dominance structure was significant for PNCV difference scores. For difONCV the ADE model with sex differences could be simplified by dropping the female dominance structure [$\Delta\chi^2(1) = 0.10$, $p = .75$], whereas the male dominance structure was significant and could not be dropped [$\Delta\chi^2(1) = 8.16$, $p = .00$]. For males, 86% of the variance in difONCV was explained by dominance genetic factors, about zero by additive genetic factors, and about 14% by unique environmental influences. For females, 87% of the variance was explained by additive genetic factors and 13% by unique environmental factors. For peak and end PNCV difference scores the *AE*-female and *ADE*-male model also was the best-fitting model. For males, the additive genetic variance in dif PNCV and difENCV was also about zero, and the dominance genetic variance 83 and 75%, respectively. For females the additive genetic variance in difPNCV and difENCV was 73 and 74%, respectively.

The correlation between onset PNCV and WAIS full-scale IQ for subjects with positive difference scores (n = 104) was .08, whereas in the other group (n = 189) the correlation was higher (.21). The results for the groups with positive and negative difference scores for peak PNCV and end PNCV were .04 (n = 169) versus .23 (n = 124) and .08 (n = 223) versus .34 (n = 70), respectively. Although the correlations between onset PNCV and IQ for the positive and negative difference score groups were not significantly different, the consistent pattern across PNCV measures of low correlations in the group with positive difference scores as opposed to higher correlations in the group with negative difference scores might support the notion that an association between PNCV and IQ becomes apparent only once PNCV has reached its highest value.

GENERAL DISCUSSION

The results of the genetic analysis of the difference scores between the PNCVs on the first and those on the second test occasion are remarkable. Nearly all of the variance in difONCV can be explained by genetic influences. These results imply that an individual's PNCV, measured on the second test occasion at age 18, is better predicted by the increase or decrease in the PNCV value of his cotwin than by his or her own PNCV score at age 16. If the difONCV value can be considered a maturation index, these results provide evidence that PNCV is still increasing for some individuals in this age interval. It might be that the variance in IQ explained by PNCV is a consequence of nerve maturation in the late adolescent years. Our data suggest that the existence of a correlation of PNCV and IQ might depend on whether nerve conduction has reached its highest value. The correlation of the Raven IQ scores measured at age 16 with PNCVs of the present study was higher then the correlation between WAIS-IQ and PNCVs of the second study. This suggests that the PNCV measures obtained at age 16 were not correlated with IQ because of ongoing maturation processes. If individual differences in PNCV become determinants of IQ only once PNCV has reached its highest value, then we would predict additional genes that influence IQ and, thus, higher heritabilities in IQ. This hypothesis of additional genetic variance is in line with the observation of further increase in IQ heritability in adults. The MZ IQ correlations appear to peak at about 16 to 20 years of age, although there are very few adult data on heritability in IQ (Bouchard, 1993).

The maturation hypothesis might explain why Vernon and Mori (1992) observed high correlations between peripheral NCV and IQ in both studies. The mean ages of their samples were 24 and 23 years, respectively. In this age group PNCV is supposed to be in a stable phase, in which the PNCV–IQ correlation can be observed. The mean age of the samples in the Barret *et al.* (1990) and the Wickett and Vernon (1994) studies was also high, but the sample sizes were too small to detect even a low significant correlation of .3. Also, the Barrett *et al.* (1990) study did not use supramaximal nerve stimulation, a requirement to make sure all nerve fibers are stimulated in the tested nerve. The mean age of the sample of the Reed and Jensen (1991) study was higher than in our own study (20 years) and the number of subjects was large (n = 200), but the absence of experimental control of temperature could be the major reason why they did not find a correlation between PNCV and IQ.

The question remains how to interpret the low but significant correlation between PNCV and IQ and the fact that this correlation is solely mediated by common genetic factors. According to Jensen and Sinha (1993), trait variation due to multiple factors (such as intelligence test scores) is unlikely to show a large correlation with any single causal factor. Small significant correlations that are consistently replicable could be of theoretical interest, especially if the intercorrelation among a number of biological and psychometric variables shows a consistent pattern. Genetic analyses are considered to play an essential role in the theoretical interpretation of intercorrelations between biological and behavioral variables. Peripheral NCV was shown to be a considerable heritable trait and the correlation with intelligence test scores, even though small, is genetically mediated. As for replicability, peripheral NCV measures for the first and present study do not correlate, and it is proposed that the reasons for this lack is based on unstable, still increasing nerve conduction velocities in the tested age interval.

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