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The Effects of Chorion Type on Variation in IQ in the NCPP Twin Population

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This investigation is part of a larger ongoing study of children who were born to mothers registered in the NINCDS Collaborative Perinatal Project (NCPP), a cooperative effort between the National Institute of Neurological and Communicative Disorders and Stroke and 12 medical centers throughout the United States. The objective of the NCPP was to observe, record, and study events which affect mothers before and during pregnancy and to relate them to their progeny. More than 50,000 pregnant women were followed through pregnancy, and the children born to these mothers were followed to 8 years of age. The collection of information, medical examinations, and laboratory tests were done in a uniform manner, according to established protocol.

The NCPP population is 45% white, 47% black, and 8% from a variety of ethnic groups, mostly Puerto Rican. The epidemiologic characteristics of twins born in the Collaborative Project have been previously described [1]. To summarize, 615 pairs of twins were born among 56,249 pregnancies with known outcome, or one in 91.5 births. The zygosity of 497 pairs was established by comparison of sex, nine polymorphic blood group systems (ABO, MNS, Rh, P, Kell, Lewis, Lutheran, Duffy, and Kidd), and gross and microscopic examination of the placenta. In 118 pairs, the zygosity could not be determined. In some pairs, one or both twins died before zygosity tests could be initiated, and placental examinations were unavailable or inconclusive. In others, the sex of one or both twins could not be determined.

There were 188 monozygotic (MZ) and 309 dizygotic (DZ) twin pairs. Among the 188 MZ pairs, 117 were monochorionic (MC) and 56 dichorionic (DC), giving a ratio of 2.09:1. In 15 pairs, the placentation could not be determined either because the placental material was unsuitable for examination or because the examination was inconclusive.

In a previous study by Myrianthopoulos et al. [2] using the NCPP data, it was found that twins performed more poorly than singletons on tests of mental and motor performance, and the detrimental effects of being a twin were greater in blacks than in

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whites. Since the twins brought up as singletons performed at the intelligence level of twins and not of singletons, the authors concluded that this lower intellectual performance is an attribute of twinning which must be associated with factors in the prenatal environment.

The importance of the human placenta with regard to the prenatal environment especially with twins, is obvious. It is a physical and physiological link between mother and child, and it exhibits variations with regard to membrane type, size, shape, and circulation which may be important in themselves or may affect the nutrition of the embryo or the transport of drugs, toxins, and other agents which can influence brain development.

This study was designed primarily to determine the effects, if any, of chorion type on the variation in IQ of MZ twins who did not have a major congenital malformation or more than one minor malformation as previously defined [1].

MATERIALS AND METHODS

At 7 years of age the NCPP children were given the Wechsler Intelligence Test for Children (WISC), which uses the following seven scales: information, comprehension, vocabulary, and digit span (verbal); and picture arrangement, block design, and coding (performance) [3]. There were 86 MZ twin pairs and 173 DZ twin pairs who had (1) no major or more than one minor congenital malformation, (2) a known chorion type, and (3) completed the 7 year WISC examination. In addition, pairs in which one or both twins had gross mental deficiency were eliminated; most of these had major malformations as well. The distribution of all twin pairs in this study by zygosity, chorion type, and race can be found in each of the tables provided with the results. The twin pairs that belonged in the "other" ethnic group were too small in number and too diverse in background to provide meaningful comparisons and thus were not included in the analyses.

The general model for the estimate of genetic variance from quantitative twin data, as previously described by Christian et al. [4], was applied to MZ and DZ twins and then separately to monochorionic and dichorionic monozygotic twins and dizygotic twins. In addition, two-tailed F tests were used to determine the equality of the among-pair and within-pair mean squares for comparisons of MC-MZ and DC-MZ IQ and DC-MZ and DZ IQ. All analyses were performed by race since nearly half the NCPP population is black, and it is well recognized that there are significant racial differences in measured IQ. The reasons for these differences and the fact that they exist at all, however, are not relevant to this study and will not be discussed.

RESULTS

The mean IQ for each of the six race-twin type classes (table 1) demonstrates that within race, there was little difference between the various twin types with regard to average IQ.

Estimates of genetic variance in whites are presented in tables 2 and 3. Using the total white MZ twin sample (table 2), we found no evidence for heterogeneity for the total variances of MZ and DZ twins ($P > .20$). In addition, the within-pair estimate (G_{WT}) of genetic variance was significantly different from zero ($P < .01$). Separating MZ twins by chorion type (table 3), we again found that the total variances were not significantly different. However, although the estimated genetic variance from comparing MC-MZ and DZ twins was significantly different from zero, the estimate from DC-MZ and DZ twins was *not* ($P > .40$).

TABLE 1

MEAN 7-YEAR IQ FOR THREE TWIN TYPES AND SINGLETONS AMONG BLACKS AND WHITES

	MC-MZ Pairs		DC-MZ Pairs		DZ Pairs	Singletons
Whites:						
No.	23		9		84	1,940
Mean	101.4		96.8		96.9	101.9
SD	14.8		15.2		13.4	13.5
		$t' = 0.82$ $P > .4$		$t' = -0.03$ $P > .9$		
Blacks:						
No.	30		24		89	1,461
Mean	85.1		84.6		85.0	91.3
SD	10.5		11.9		13.1	12.6
		$t' = 0.18$ $P > .8$		$t' = -0.16$ $P > .8$		

NOTE.—Differences between the means were determined using the t' test in the manner suggested by Christian and Norton [10].

TABLE 2

IQ: ESTIMATE OF GENETIC VARIANCE FROM WHITE MZ AND DZ TWIN PAIRS

	MZ (32 PAIRS)		DZ (84 PAIRS)	
SOURCE	Mean Squares	df*	Mean Squares	df
Among	418.46	31	274.11	83
Within	37.09	32	83.67	84
Test of Twin Model:				
Sum of mean squares	455.55	36.5	357.77	129.5
		$F' = 1.27$		
		$P > .20$		

NOTE.—Estimate of genetic variance: $\hat{G}_{WT}$ = Within MS_{DZ} − Within MS_{MZ} = 46.57, $F = 2.26$ ($P < .01$).
* df = degrees of freedom.

Estimates of genetic variance in blacks are presented in tables 4 and 5. Using the total black MZ twin sample (table 4), we found some evidence for heterogeneity for the total variances ($P < .20$) of MZ and DZ twins [4]. Consequently, we used the arithmetic mean of within-pair and among-pair estimates (G_{CT}) to estimate twin genetic variance. This estimate was *not* significantly different from zero ($P > .25$). Separating MZ twins by chorion type (table 5), we found some evidence for heterogeneity between the MC-MZ and DZ total variances ($P < .20$) but not between the DC-MZ and DZ total variances ($P > .20$). Although the estimated genetic variance comparing MC-MZ and DZ twins was not significantly different from zero ($P > .25$), the estimate comparing DC-MZ and DZ twins *was* ($P < .01$).

Again, performed by race, two-tailed F tests for homogeneity of variance revealed a significantly greater within-pair mean square for white DC-MZ twins than white MC-DZ twins ($F_{9,23} = 3.33$, $P < .01$). The black DC-MZ twins had a larger within-pair mean square than the black MC-MZ twins, but the difference was not significant ($F_{24,30} = 1.35$, $P > .2$). Comparisons of among-pair mean squares by race revealed no evidence of heterogeneity. A comparison of DC-MZ and DZ pairs revealed a significantly greater within-pair mean square for black DZ twins than black DC-MZ twins ($F_{89,24} = 2.37$, $P < .01$). The white DC-MZ and DZ within-pair mean squares, however, were quite similar ($F_{84,9} = 1.12$, $P > .4$). Again comparisons of among-pair mean squares by race revealed no evidence of heterogeneity.

DISCUSSION

The results of this study indicate that within race the zygosity and/or chorion type had little effect on the overall mean IQ. However, the observed within-pair measure of IQ in whites indicates that members of dichorionic-monozygotic pairs are significantly more discordant than members of monochorionic-monozygotic pairs ($P < .01$). This was not true for blacks, although the same trend was evident. This heterogeneity in the within-pair variation of monochorionic and dichorionic MZ twins suggests that as a group there are two populations of MZ twins with regard to variation in IQ. It also implies a rather considerable influence of the prenatal environment on this measure of intelligence, which is associated with the uniqueness of one or both of the chorion types involved.

TABLE 3

IQ: ESTIMATES OF GENETIC VARIANCE BY CHORION TYPE FROM WHITE TWINS

SOURCE	MC-MZ (23 PAIRS)		DZ (84 PAIRS)		DC-MZ (9 PAIRS)	
	Mean Squares	df*	Mean Squares	df	Mean Squares	df
Among	427.38	22	274.11	83	410.14	8
Within	22.39	23	83.67	84	74.67	9
Test of Twin Model:						
Sum of mean squares	449.77	24.3	357.78	129.5	484.81	10.9
			$F' = 1.26$		$F' = 1.36$	
			$P > .20$		$P > .40$	

NOTE.—Estimates of genetic variance: (1) $\hat{G}_{WT}$ = Within MS_{DZ} − Within MS_{MC-MZ} = 61.28, $F = 3.73$ ($P < .001$); (2) $\hat{G}_{WT}$ = Within MS_{DZ} − Within MS_{DC-MZ} = 9.00, $F = 1.12$ ($P > .40$).

* df = degrees of freedom.

TABLE 4

IQ: ESTIMATE OF GENETIC VARIANCE FROM BLACK MZ AND DZ TWIN PAIRS

Source	MZ (54 Pairs)		DZ (89 Pairs)	
	Mean Squares	df*	Mean Squares	df
Among	211.62	53	248.72	88
Within	35.03	54	97.16	89
Test of Twin Model:				
Sum of mean squares	246.65	70.1	345.87	147.9
		$F' = 1.40$ $P < .20$		

NOTE.—Estimate of genetic variance: $\hat{G}_{CT} = \hat{G}_{AT} + \hat{G}_{WT}/2 = 12.52, F = 1.09\ (P > .25)$.
* df = degrees of freedom.

We were fortunate in this study to have had an accurately determined population of DC-MZ twin pairs in which, we are reasonably confident ($.003 < P < .04$), there are no misclassified dizygotic twins. This allowed us to make the important comparisons between dichorionic MZ and DZ twin pairs. Surprisingly, in whites the within-pair variations of these two groups were not significantly different ($P > .4$). They were, however, in blacks ($P < .01$).

As Corey et al. [5] point out, the effects of prenatal environment associated with the chorion types either have a different environmental variance, a different environmental covariance, or both. These differences can introduce a serious and systematic bias in the interpretation of twin data since it represents a source of extraneous variation in comparisons of MZ and DZ twins. This is clearly evident in the data presented here (tables 3 and 5). Our results suggest that twin studies which have determined a high heritability in whites and a low heritability in blacks for measured IQ [6, 7] may be seriously biased by the proportion of each chorion type in their monozygous twin cohort. For example, if one restricts heritability studies to MZ and DZ twins with "equivalent" prenatal environments (i.e., only DC-MZ twins), then our data would indicate that blacks, *not* whites, have a significant genetic component of variance.

Viewed in its totality, then, these data suggest to us that, at least in white twin pairs, dichorionic placentas are of greater influence than the similarity or dissimilarity of genomes vis-à-vis intrapair IQ measurements at age 7. The biologic basis for the importance of the dichorionic placenta is not clear.

Bulmer [8] claims that the interconnected fetal circulation in monochorionic twins is an inefficient vascular arrangement. In addition, he points out that between 15% and 30% of monochorionic twins suffer from the "transfusion syndrome" in which an uncompensated arterio-venous shunt leaves one twin plethoric and the other pale and anemic. Since the hemoglobin content and thus oxygen carrying capacity is decreased in one of a pair of such monochorionic twins 15%–30% of the time and since oxygen is needed in large amounts for rapidly dividing cells such as neural cells, it would seem, a priori, that the intrapair variation of IQ in monochorionic twins might be considerable. Apparently, either the frequency or the degrees of severity of the consequences of the transfusion syndrome or both have been overestimated. Perhaps

TABLE 5

IQ: Estimates of Genetic Variance by Chorion Type from Black Twins

Source	MC-MZ (30 Pairs)		DZ (89 Pairs)		DC-MZ (24 Pairs)	
	Mean Squares	df*	Mean Squares	df	Mean Squares	df
Among	191.44	29	248.72	88	245.94	23
Within	30.28	30	97.16	89	40.96	24
Test of Twin Model:						
Sum of mean squares	221.72	38.0	345.87	147.9	286.90	30.5
			$F' = 1.56$ $P < .20$		$F' = 1.21$ $P > .20$	

Note.—Estimates of genetic variance: (1) MC-MZ and DZ: $\hat{G}_{CT} = \hat{G}_{AT} + \hat{G}_{WT}/2 = 4.80$, $F = 1.03$ ($P > .25$); (2) DC-MZ and DZ: $\hat{G}_{WT} = WMS_{DZ} - WMS_{DC-MZ} = 56.20$, $F = 2.37$ ($P < .01$).

* df = degrees of freedom.

the latter is the case, and the transfusion syndrome is of much less importance than competition between dichorionic placentas. This view is supported by the data of Rausen et al. [9] who found that although 15% of the monochorionic twin pairs suffered from the transfusion syndrome at birth, in only 20% of these did both twins of a pair survive past infancy or 3% of the original population of monochorionic twin pairs. Thus only a very small number of such twins is likely to have been available at age 7 for IQ testing and subsequent inclusion in this study.

Corey et al. [5] offer an interesting hypothesis for the unexpected findings such as we found in the white twins. They maintain that because there is likely to be developmental asynchrony in twin embryos sharing the same uterus, presumably this could lead to unequal competition for and/or distribution of essential metabolites and thus twin discordance. They reason that such asynchrony would be minimized by the single placenta and circulatory anastomosis of monochorionic twins; however, this would not be so for dichorionic twins because of their physical and/or circulatory independence. Although this hypothesis is tenable, it remains ad hoc since they offer no means of testing it in humans or other animals for that matter.

We would like to present an alternative hypothesis which can be tested. Monochorionic twins have a single implantation and placenta, while dichorionic twins, depending on whether the embryos become implanted close together or far apart, have either two separate placentas (60%) or a single placenta formed by the fusion of the two original placentas (40%) [8]. This leads to a rather simple observation and set of predictions. If the general incidence or probability of placental anomalies (x) is found to be $^1/_5$, for example, then the a priori probability of a single placenta being anomalous is $^1/_5$, but the a priori probability of one of a given pair being anomalous is $^8/_{25}$ or nearly $^1/_3$. Thus, when $x = {}^1/_5$, the a priori probability of one of a pair of dichorionic placentas being anomalous is 1½ times the a priori probability of a monochorionic placenta being anomalous.

This observation leads to at least three reasonable predictions. (1) The frequency of placental anomalies in a monochorionic pair will be less than that in a dichorionic pair. (2) A pair of dichorionic twins discordant for a particular quantitative trait is more likely to have a placental anomaly than a concordant pair. In the case of IQ, the dichorionic twin with the placental anomaly is more likely to have the lower IQ. (3) Monochorionic pairs with a placental anomaly will not necessarily be more discordant than a pair without such an anomaly since both types of monochorionic pairs would still share a common placenta and interconnected fetal circulation. They would also be subjected relatively equally to the competition for and/or Poissonian distribution of essential metabolites. These predictions are currently being tested in the NCPP twin population.

SUMMARY

The 7-year IQ scores (WISC) of 116 white and 143 black nonmalformed twins of known zygosity and placental type were ascertained from the NINCDS Collaborative Perinatal Project (NCPP). The type of chorion and zygosity had no significant effect on the mean IQ or among-pair variation. In white monozygotic twins, however, analysis of variance revealed a significantly greater within-pair mean square for dichorionic

twins than monochorionic twins. On the other hand, the white dichorionic monozygotic (MZ) and dizygotic (DZ) within-pair mean squares were quite similar. These findings were not evident in blacks for either of the within-pair comparisons. In addition, estimates of genetic variance were dependent upon MZ chorion type in both races. These data suggest to us that (1) in white twin pairs dichorionic placentas are of greater influence than the similarity or dissimilarity of genomes with regard to intrapair IQ development, and (2) failure to consider chorion type may introduce a serious bias in the interpretation of genetic variance estimates of IQ variability.

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