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A Family Study of Developmental Effects upon Blood Pressure Variation

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Abstract. In an earlier study of blood pressure variation in middle aged parents and their young adult twin offspring, the greater blood pressure variation observed in the parent sample was accounted for in terms of an increasing influence of individual environmental experiences with increasing age and a commensurate reduction in the impact of heredity. In the present study, the sample size was enlarged to provide a more powerful test of these effects. Maximum likelihood model-fitting techniques were applied to blood pressure covariation in balanced pedigrees, consisting of 85 families (40 MZ and 45 DZ twin pairs). As before, our analysis indicated that a developmental effect was a salient factor in the older age group.

Key words: Blood pressure, Twin family design, Heredity, Age, Developmental effects, Individual environment

INTRODUCTION

It is now well established that hereditary factors account for much of the familial aggregation of blood pressure (BP) [9,10]. As much as 60% of the total variance seems to be attributable to genetic factors [5]. However, this implies that environmental influences may still account for at least 40% of BP variability. In addition, little attention has been given to the possibility of changing genetic and environmental contributions with aging. Such analysis could be important in determining precursors of hypertension [12,13].

Recent research in our laboratory is pertinent here [15]. No simple genetic or environmental model was adequate to explain the pattern of BP variation observed in our sample of young twins and their middle-aged parents. This was largely due to an increase

in BP variation from young adulthood to middle age. Only models which allowed for a developmental effect, whereby the influence of individual environmental factors increased with advancing age, were adequate to account for our data.

The present study reports the findings from an enlarged sample of twins and their parents. This should afford a much more powerful test of the effects seen in the original study.

METHOD

Subjects

The original sample comprised 57 complete families (25 MZ and 32 DZ families). For the present study, a further 28 families were tested, comprising 15 MZ and 13 DZ twin families; hence, 85 complete families were available for analysis. The mean age of the twins in the enlarged sample was 19.38 years (SD 3 years). The parents were middle aged (mothers' mean age = 49.1 years, SD 6 years; fathers' mean age = 51.5 years, SD 6 years). The subjects were all recruited from the population-based Birmingham Family Study Register.

Procedure

The procedure was identical to that used in the original study. All BPs were monitored from seated subjects by the same researcher (JS), using a standard sphygmomanometer and stethoscope. BP readings in the twins were taken during a laboratory psychophysiological testing session. The details of this are described in full elsewhere [2]. After a period of about 20 minutes for acclimatization to the laboratory, two initial BP readings were taken. Two final readings were taken, approximately two hours later.

The twins' parents were visited in their homes. Two initial BP readings were taken, followed by two more, approximately 90 minutes later. Where parents were diagnosed hypertensives, receiving antihypertensive medication, a BP value of 150/90 was entered for the purposes of analysis. This was the case for one mother and one father of MZ twins and six mothers and four fathers of DZ twins. Such exceptions aside, all four readings were averaged for each subject, to yield composite systolic and diastolic BP values. These composite values were subsequently used in the analysis.

Model Fitting

The variance-covariance matrix for each family type was entered into a "Lisrel VI" Fortran program [11]. The program affords best estimates of the genetic and environmental parameters in the proposed models, together with their standard errors, chi-square goodness of fit statistics for the model, degrees of freedom and the probability of observing the data given the model and the parameter estimates. Details are presented in the original paper [15]. There were 4 variances and 6 covariances for both systolic and diastolic BP; these appear in Tables 1 and 2.

Table 1 - Covariance and correlation matrices for diastolic blood pressure[a]

	Elder twin	Younger twin	Mother	Father
MZ twins (N =40 families)				
Elder twin	89.79	0.60	0.36	0.19
Younger twin	54.57	94.71	0.33	0.16
Mother	57.71	54.59	284.60	0.12
Father	27.45	23.68	31.59	225.05
DZ twins (N =45 families)				
Elder twin	127.61	0.42	0.25	0.27
Younger twin	52.59	124.88	0.35	0.40
Mother	49.31	68.49	312.81	0.10
Father	59.34	85.41	33.08	366.06

[a] Variances are given on the leading diagonal of each of the two 4 x 4 matrices, covariances in the lower triangle and correlations in the upper off-diagonal entries.

Table 2 - Covariance and correlation matrices for systolic blood pressure[a]

	Elder twin	Younger twin	Mother	Father
MZ twins (N =40 families)				
Elder twin	83.62	0.83	0.20	0.12
Younger twin	66.68	77.11	0.27	0.10
Mother	19.04	25.19	108.32	0.11
Father	11.92	9.47	12.14	112.64
DZ twins (N =45 families)				
Elder twin	47.34	0.51	0.30	0.32
Younger twin	22.19	40.24	0.13	0.32
Mother	21.80	8.56	108.04	- 0.005
Father	22.26	20.48	- 0.50	101.30

[a] Variances are given on the leading diagonal of each of the two 4 x 4 matrices, covariances in the lower triangle and correlations in the upper off-diagonal entries.

RESULTS

Concordance for BP was high. Product-moment correlations for MZ twins were 0.60 and 0.83 for systolic and diastolic BP respectively. The corresponding figures for DZ twins were 0.42 and 0.51. These figures compare well with those reported by other researchers [1,6,14,16].

For systolic BP, variance for the parents was approximately two and a half times

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Table 3 - Mean systolic and diastolic blood pressures in MZ and DZ twins and their parents

	MZ twins		DZ twins	
	Mean SBP	Mean DBP	Mean SBP	Mean DBP
Elder twin	121.47	80.02	125.73	80.80
Younger twin	119.82	78.37	122.82	79.62
Mother	125.85	83.30	125.31	82.68
Father	132.65	87.97	133.40	86.71

greater than that observed for their twin offspring. Diastolic BP variance was almost twice as great in the parent sample. Analogous differences have been reported elsewhere [3,4,7,8]. The respective mean BP values indicated that this was not a simple scalar effect; mean maternal BP values were similar in magnitude to the sons and the elevation in the paternal mean was less than 10% (Table 3).

Model Fitting

Tables 4 and 5 show the results of model fitting for diastolic and systolic BP respectively.

Table 4 - The results of fitting genetic and environmental models to diastolic blood pressure

Model	Variance estimate θ	SE	df	χ^2	P
1. E1	84.18	3.27	19	95.43	0.000
2. E1	25.35	2.15	18	49.68	0.000
Dr	130.25	9.48			
3. E1	18.64	1.44	18	34.60	0.011
E2 (dev.)	71.09	4.04			
4. E1	114.77	5.14	18	103.07	0.000
E2 (family)	26.98	4.51			
5. E1 twin	60.98	3.35	18	82.31	0.000
E1 parent	107.40	5.89			
6. E1 twin	12.78	1.37	17	16.01	0.523
E1 parent	71.79	6.01			
Dr	84.19	7.01			
7. E1 twin	17.88	1.39	17	24.84	0.098
E1 parent	64.27	7.18			
E2 (dev.)	43.11	4.10			
8. E1 twin	21.85	1.63	17	32.08	0.015
E1 parent	102.37	6.03			
E2 (family)	33.12	3.32			
9. E1	12.20	1.34	16	14.10	0.592
Dr twin	87.73	7.35			
Dr parent	189.42	33.12			
Dr twin/parent	62.39	18.38			

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Table 5 - The results of fitting genetic and environmental models to systolic blood pressure

Model	Variance estimate θ	SE	df	χ^2	P
1. E1	202.24	7.85	19	91.24	0.000
2. E1	72.88	6.38	18	54.21	0.000
Dr	283.42	22.85			
3. E1	62.62	4.82	18	60.92	0.000
E2 (dev)	158.34	10.12			
4. E1	151.86	6.80	18	66.27	0.000
E2 (family)	50.31	7.06			
5. E1 twin	110.27	6.05	18	52.81	0.000
E1 parent	294.11	16.14			
6. E1 twin	35.81	3.74	17	8.16	0.963
E1 parent	222.815	16.52			
Dr	153.97	14.65			
7. E1 twin	56.75	4.40	17	30.51	0.023
E1 parent	240.59	17.49			
E2 (dev)	53.52	6.73			
8. E1 twin	56.33	4.12	17	9.66	0.917
E1 parent	243.06	14.27			
E2 (family)	53.38	6.07			
9. E1	38.18	4.07	16	6.69	0.979
Dr twin	143.17	14.74			
Dr parent	510.15	33.28			
Dr twin/parent	192.96	36.68			

Diastolic BP

At the outset, purely environmental models were tested. Model 1 attributes all variation to individual environmental effects. Model 3 includes environmental effects shared by offspring during development. This assumes that the impact of such effects is not shared by the parents. Model 4 includes those environmental effects shared by the whole family (eg, cultural effects). In all these models, variance is assumed to be equivalent for both age groups. In Model 5, however, offspring and parents are allowed to take different values for individual environmental variance. None of these models adequately fitted the data.

A simple additive genetic, within family environmental effects model was tested next (Model 2), but it too was inadequate. However, Model 2 does not allow for changing BP variance across generations. Further models, 6 to 9, do. Model 6 was adequate to account for the data ($P < 0.5$). It assumes: different individual environmental influences with aging; fixed, simple additive genetic effects; no assortative mating and no shared developmental or cultural environmental effects. Model 7, which includes shared developmental effects as well as changing individual environmental effects was also statistically adequate in fit ($P > 0.05$). The other purely environmental model, Model 8, was rejected ($P < 0.05$). Model 9, a four parameter model, also fitted the data well ($P > 0.5$). Here, the environmental impact was held constant whilst the genetic influence was separated into

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twin and parent variation and also twin-parent covariation. However, the principle of parsimony precludes adoption of this model for the present.

Systolic BP

As with diastolic BP, the main reason for the failure of simple genetic and environmental models seemed to be the exclusion of the increasing BP variance with age effect. Hence, for systolic BP, Models 6 and 9 again most adequately accounted for the observed data ($P > 0.9$). Model 8, where a shared family environmental effect was included also fitted the data ($P > 0.9$).

Since MZ correlations and covariances differed from those of DZ, a purely environmental model would not be feasible. A model allowing for genetic effects would be adopted in preference.

DISCUSSION AND CONCLUSIONS

The present study affords further evidence of familial aggregation of BP. However, no simple environmental or genetic model was adequate to account for the observed pattern of BP variation. As in our previous, more limited study, there was a developmental trend; BP variation increased with age. Thus, only models which allowed for such changes accorded with our data. Model fitting once more revealed changing genetic and environmental contributions with aging. Individual environment was revealed as a salient factor with increasing age. The parameter estimates in Model 6 reveal an over five-fold increase in the impact of individual environment from young adulthood to middle age. Commensurately, BP heritability estimates decreased from 6% for the offspring to 37% for the parents for diastolic BP and from 68% to 25% for systolic BP.

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