Exclusion Distorts Heritability Estimates of Ambulatory Blood Pressure

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Introduction

Genetics of ABP may differ from that of conventional blood pressure, however, because it is unaffected by the 'white-coat' effect. To date, only few twin and family studies have examined the heritability of ambulatory blood pressure (ABP). Most twin and family studies of ABP have excluded subjects taking antihypertensive medication or have performed their analyses on normotensive subjects only, thereby removing an important part of the population variance of interest (Cui et al., 2003).

The present study examined the impact of excluding hypertensive and/or medicated subjects on the estimates of genetic influences on ambulatory systolic (SBP) and diastolic blood pressure (DBP).

Methods

- Sample

  230 MZ twins (85 men), 305 DZ twins (111 men) and 257 singleton siblings (98 men) from 339 families

- Procedure

  Subjects wore a Spacelabs 90207 ambulatory BP monitor, with arm-size appropriate cuff during day time. Measurements took place every 30 (±10) min. In case of a misreading BP was measured again 2 min. later

  A diary was kept every 30 minutes to get a chronological account of e.g. posture, activities, social situation

  Genetic analyses were performed twice:

  1. Analysis under strict exclusion (medication and/or BP > 135/85)

  2. Ana.lysis without any exclusion. Published efficacy of their specific antihypertensive drugs (Mancia, G. & Parati, G., 2004) were used to estimate untreated blood pressure values in medicated subjects.

- Data reduction

  We computed mean SBP and DBP across all readings in the morning, afternoon and evening.

- Statistical analyses

  Mx was used for biometrical model fitting. Variance was decomposed into additive genetic (A), common environmental (C) and unique environmental sources of variance (E). These components for tested for significance. Trivariate models were evaluated with maximum likelihood tests.

Results

The histograms in figure 1 show the distributions of SBP (a&b) and DBP (c&d) in the restricted and unrestricted dataset. In the restricted dataset means are reduced by 2-5% and standard deviations by 30-39%.

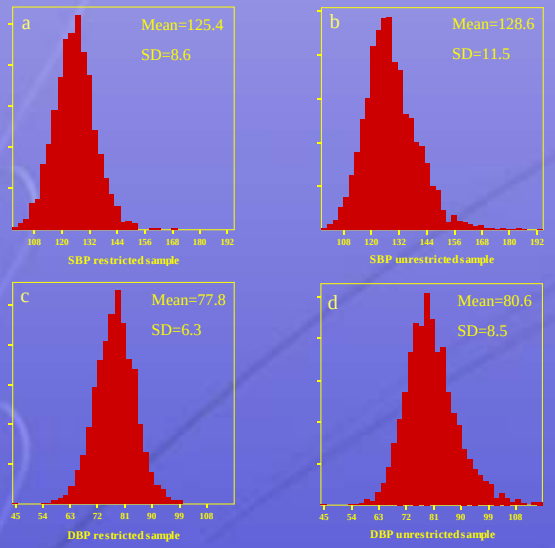

Figure 1a-d Distributions of SBP and DBP for both datasets

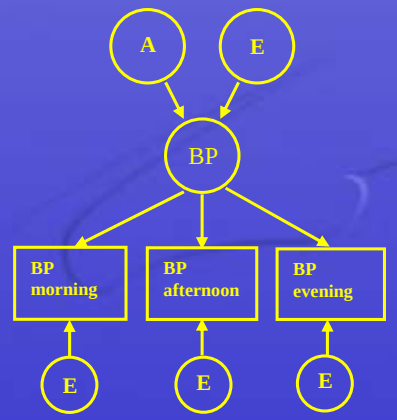

Figure 2 Common pathway AE model

The best fitting model was a common pathway AE model in which A and E influence the three measures through a common latent phenotype (BP), while allowing for specific E at all measurement periods (see figure 2). Table 1 shows the heritability estimates for both the restricted and unrestricted dataset. Restricting the dataset by exclusion of hypertensive and/or medicated subjects decreases heritability estimates with 8-15% for DBP and with 7-12% for SBP.

TABLE 1 Heritability Estimates for SBP and DBP

Restricted dataset	Common pathway		Specific
	A	E	E
DBP	40-55%	17-30%	37-52%
SBP	32-50%	34-38%	12-44%

Unrestricted dataset	Common pathway		Specific
	A	E	E
DBP	46-63%	19-27%	10-35%
SBP	44-57%	27-34%	9-29%

Conclusion & Discussion

A substantial part of the genetic variance in ABP is lost when excluding hypertensive (and/or medicated) subjects. Since blood pressure most likely is a polygenic trait, with many small QTL effects, statistical power should be maximized. Therefore, exclusion of hypertensive and/or medicated subjects should be avoided in future gene finding and linkage studies.

References

Cui, J. S., Hopper, J. L., & Harrap, S. B. (2003). Antihypertensive Treatments Obscure Familial Contributions to Blood Pressure Variation. *Hypertension, 41*, 207-210.

Mancia, G. & Parati, G. (2004). Office compared with ambulatory blood pressure in assessing response to antihypertensive treatment: a meta-analysis. J.Hypertens., 22, 435-445.