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 a 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 daytime. 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. Analysis 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 were tested for significance. Trivariate models were evaluated with maximum likelihood tests.

Results

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

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.

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
