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Influences of Familial and Environmental Factors on Hypertension

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ABSTRACT

A group of 293 middle-aged subjects with a parental history of hypertension was compared with 210 middle-aged subjects without this history. The adjusted odds ratio for hypertension (WHO-criteria) was 2.0 with parental hypertension - independent of obesity, physical leisure time activity, age and sex. Comparatively in all 503 participants, the independent odds ratio for hypertension was 3.3 with obesity.

Analysis of variance in all participants disclosed that blood pressure was independently related to three predictors, parental hypertension ($p < 0.05$), body mass index ($p < 0.001$), and 2-h blood glucose ($p < 0.001$).

Additional analysis of variance in all subjects, to estimate if these three predictors were interrelated, disclosed that parental hypertension was not related to either 2-h glucose or body mass index. A clear association was seen between 2-h glucose and body mass index ($p < 0.001$). This was underlined in a separate analysis of the 88 hypertensives, among which 25 % had impaired glucose tolerance (WHO-criteria).

In conclusion, own obesity (environment) had about 1.5 times stronger influence on hypertension than parental hypertension (heredity). Parental hypertension seemed to have a separate influence on the blood pressure. Body mass index and 2-h glucose seemed to have partly separate, and partly interrelated, influences on the blood pressure.

INTRODUCTION

Essential hypertension has been shown to aggregate within families, suggesting a possible role of hereditary factors (5,6,13,14,19). Furthermore, hypertension has been related to possible environmental factors, like obesity and low physical fitness (1,9,13,16). Few studies, however, have evaluated the relative influence by either familial hypertension or obesity (5,6,19), and if these two predictors are independent or co-operating (5,13).

It was the aim of this study to estimate, in a Swedish population, the degree of influence on hypertension by either parental hypertension or obesity, and also to estimate if these two influencing factors were interrelated to hyperglycaemia.

MATERIAL AND METHODS

The material of this study consisted of 503 subjects (301 females and 202 males), 293 subjects with a positive family history of hypertension and 210 subjects without this history. The subjects were a sample of middle-aged, 47-52 years old, inhabitants in the city of Uppsala, participating in an epidemiologic study of impaired glucose tolerance (IGT) and hypertension (1). In the present study, the exclusion criteria were manifest diabetes mellitus and lack of knowledge of parental hypertension.

Blood pressure (BP) was measured casually at rest in the sitting position with Korotkoff fifth phase sounds with a mercury manometer and a cuff size 12.5 x 35 cm. According to WHO-criteria, hypertensive subjects (n=88) were defined as those previously on antihypertensive treatment (n=68) or those with untreated systolic BP $\geq$160 mm Hg and/or diastolic BP $\geq$95 mm Hg (n=20) at the study. Mean BP was calculated as diastolic BP + one-third of pulse pressure (systolic - diastolic BP).

Body mass index (BMI) was computed by dividing weight with indoor clothing by the square of height without shoes ($kg \cdot m^{-2}$). Relative BMI (%) was expressed from standard BMI values according to the Society of Actuaries (8) for comparison between sexes. Obesity (n=185) was defined as RBMI $\geq$120%.

Oral glucose tolerance tests were performed with 75 g glucose loads in the morning after 10 hours of fasting, according to WHO prescriptions (18). Venous whole blood glucose was measured at 0-h and 2-h levels by a glucose oxidase method (Yellow Spring Instrument Model 23 AM). IGT-subjects (n=50) were diagnosed (WHO-criteria), on the basis of two subsequent tolerance tests, as those with: 0-h glucose <6.7 $mmol \cdot l^{-1}$ and 2-h glucose 6.7 - <10.0 $mmol \cdot l^{-1}$ (18).

The participants were asked 'Do/did your mother/father have hypertension?: Yes / No / Don't know'. Subjects having at least one parent with hypertension formed the group with a family history of hypertension. Subjects who definitely reported no hypertensive father and no hypertensive mother formed the group with no parental hypertension. Subjects were excluded from the study if they lacked knowledge about both parents, or lacked knowledge of one parent when the other was normotensive.

Physical leisure time activity (PLTA) was evaluated with use of a 4-point scale at a questionnaire, representing the mean daily activity during the last year, found to be significantly related to maximal oxygen uptake (4). PLTA

groups 1 and 2 formed the low PLTA group at the statistical analysis (n=423), while PLTA groups 3 and 4 formed the high PLTA group (n=80).

STATISTICAL ANALYSIS

Statistical analyses were carried out with the SAS program package (SAS Institute Inc., N.C., USA). A p value of <0.05 was considered to be statistically significant. Mean values were given with SE. Analysis of covariance (PROC GLM) was used to adjust all mean values for age and sex. Spearman's correlations were performed with variables treated as 0 or 1. Analysis of variance (PROC GLM) yielded the F-value of each independent predictor, with the coefficient of determination (R^2).

Analysis of the frequency distribution (PROC FREQ) was carried out for two or n variables. Two-way analysis yielded frequency figures (%), with computation of simple chi-square statistics. N-way analysis yielded the odds ratio with 95% confidence limits, and included computation of Cochran-Mantel-Haenszel correlation and general association statistics. By this method the odds ratio (or relative risk) was adjusted for n confounding covariates.

RESULTS

Table 1. Subjects with or without parental hypertension (MV±SE, %)

	With parental HT	Without parental HT
Numbers	293	210
Systolic BP (mm Hg)	135±0.8 **	131±0.9
Diastolic BP (mm Hg)	84±0.4	83±0.5
Mean BP (mm Hg)	101±0.5 **	99±0.6
Hypertension (%)	21.8 **	11.4
0-h glucose ($mmol \cdot l^{-1}$)	4.4±0.03	4.4±0.03
2-h glucose ($mmol \cdot l^{-1}$)	4.6±0.09	4.5±0.11
Impaired glucose tolerance (%)	11.3	8.1
Relative BMI (%)	120±1	118±1
Obesity (relative BMI ≥120%) (%)	39.6	32.9
Low physical leisure activity (%)	82.9	85.7
Age (years)	51±0.2	51±0.2
Females/males (%)	62/38	57/43

Significance levels: *** P <0.001, ** p <00.01, * p <0.05. HT=hypertension.

The prevalence of hypertension (Table 1) was higher in subjects with a parental history of hypertension, 22%, than in those without, 11%. Systolic and mean BP values (adjusted for age and sex) were also higher with parental hypertensionthan without. No differences were seen between these two groups concerning BMI, blood glucose or PLTA.

Analysing all 503 participants, obese subjects had more hypertension than non-obese, 32% versus 9% ($p < 0.001$). Furthermore, subjects with low PLTA had more hypertension than those with high PLTA, 19% versus 9 % ($p < 0.05$). Table 2 shows independent odds ratios for hypertension, adjusted for the confounding effect of covariates. Odds ratios were increased with parental hypertension, 2.0, with obesity 3.3, and with low PLTA, 2.4.

Table 2 also shows Spearman's coefficients between hypertensive parent and hypertensive offspring, also after subdividing into father or mother, and son or daughter. The coefficient concerning parent - offspring was r=0.14, and r=0.11 -0.16 in the subdivided groups.

Analysis of variance in all 503 participants (Table 3) showed that blood pressure as dependent variable was independently related to BMI, to parental hypertension, and also to 2-h blood glucose.

As we also intended to analyse if these three predictors were interrelated, 2-h glucose was held as dependent variable in a subsequent analysis of variance in all participants (Table 3). We found 2-h glucose strongly related to BMI, but 2-h glucose was not related to parental hypertension. With BMI held as dependent

Table 2. Adjusted odds ratios with 95% limits for hypertension (HT), with parental hypertension, obesity or physical leisure time activity (PLTA). Spearman's correlations between hypertensive parent (mother, father) and hypertensive offspring (son, daughter).

	Odds ratio (95% limits)	Corr. coeff.	Families
Obesity [&]	3.3 (2.0-5.5) ***	-	503
Low PLTA [$]	2.4 (0.9-6.1)	-	503
Parental hypertension [§]	2.0 (1.1-3.4) *	0.14 **	503
Mother HT - son HT [§]	2.7 (1.0-7.3) *	0.16 *	194
Mother HT - daughter HT [§]	1.9 (1.0-3.6) *	0.13	290
Father HT - son HT [§]	2.2 (0.8-8.5)	0.15 *	172
Father HT - daughter HT [§]	1.5 (0.7-3.0)	0.11	254

Significance levels: *** pp <0.001, ** p <0.01, * p <0.05.
Adjusted for: [&] parental HT-PLTA-age-sex; [$] parental HT-obesity-age-sex;
[§] obesity-PLTA-age-sex.

Table 3. Analysis of variance (F-values) between blood pressure (BP) or 2-h glucose as dependent variables, versus various predictors, n=503.

	Dependent variables:			
	Systolic BP	Diastolic BP	Mean BP	2-h glucose
Predictors:				
Relative BMI	23.5 ***	22.4 ***	27.9 ***	68.0 ***
Parental hypertension	9.0 *	2.4	5.1 *	0.1
2-h blood glucose	28.5 ***	16.7 ***	26.8 ***	-
Physical leisure activity	3.5	4.8 *	5.1 *	3.3
Age	17.9 ***	2.0	9.4 *	1.7
Sex	3.7	3.2	4.1 *	0.8
R	0.20	0.13	0.19	0.15

Significance levels: *** p <0.001, ** p <0.01, * p <0.05. R =coeff. determ.

variable, parental hypertension was not related to BMI (not given in the Table).

We also analysed the 88 hypertensives separately (not given in the Table). Twenty-five per cent of the hypertensives had IGT. The hypertensive group also had a strong association between 2-h glucose and BMI (p <0.001), but no association between 2-h glucose and parental hypertension. The hypertensives with IGT had a similar frequency of anti-hypertensive agents as the hypertensives with normal glucose tolerance, 73% versus 78 % (ns), mainly thiazides and beta-adrenergic blockers.

Finally in a subgroup (Table 4), the odds ratio for hypertension was 9.1 with the simultaneous presence of parental hypertension and obesity.

Table 4. Odds ratios with 95% limits (adjusted for physical activity, age, sex) for hypertension with either parental hypertension (PHT), obesity or both.

	Odds ratio (95% limits)
PHT and nonobese (n=177) / no PHT and nonobese (n=141)	3.0 (1.1-8.0) *
No PHT and obese (n=69) / no PHT and nonobese (n=141)	4.8 (1.8-13.0)**
PHT and obese (n=116) / no PHT and nonobese (n=141)	9.1 (4.1-20.1)***

Significance levels: *** p <0.001, ** p <0.01, * p <0.05.

DISCUSSION

We found that the relative risk for hypertension was 2.0 with parental hypertension. Similarly, the likelihood of hypertension has previously been reported to be twice as high with parental hypertension than without (14). Our statistical method allowed us to estimate the relative risk, independent of obesity, physical activity, age or sex.

In the present study, parental hypertension was also independently related to high BP levels in offspring. Notably, the F-value for parental hypertension in our study had a relative strength, that was comparable to that of the F-value for parental BP level in Framingham, when they related offspring BP to parental BP, BMI and some biochemical predictors (5). We also estimated the correlation between hypertension in parent and hypertension (or BP level) in offspring, $r = 0.14$. Similarly in Framingham, the general correlation between parental BP and offspring BP was $r=0.15$ (5). These agreements with Framingham should fairly well mitigate the possible bias of too high reports of parental hypertension in treated hypertensives, and implied that parental history was possible to use in the analysis.

We found no obvious difference when correlating with maternal or paternal hypertension, $r=0.11-0.16$. Comparable results were obtained in Gothenburg between maternal or paternal BP levels versus BP levels in sons (17).

Familial aggregation can be due to both heredity and to intrafamilial environment. However, studies in Framingham, Tecumseh and Utah, correlating BP levels of parents and offspring, found that shared familial environment explained only about 5% of the variance of the hypertensive phenotype. Shared genes explained about 50% (up to 65% in Utah twins) (5,6,19). Accordingly, we have regarded a parental history of hypertension as a mainly hereditary variable in this study.

Concerning obesity, a hereditary influence on body weight has been suggested in recent twin studies (15). However, no correlation was seen in Gothenburg between BMI values of about 60-years-old parents and 30-years-old offspring (17). Likewise, we did not find significant associations between familial NIDDM (patients with NIDDM per se often obese) and BMI in offspring (not given in Table). Therefore, BMI was regarded here as a mainly environmental factor.

It is well established that hypertension is more prevalent in obese than in nonobese subjects (1,13,16). Possible environmental links exist between obesity and hypertension, such as increased salt intake with the food, and hyperinsulinemia (3,7). We found here that the independent relative risk for hypertension was 3.3 with obesity. This finding was somewhat contrary to the cited estimates, that heredity was responsible for 50%, and environment or to some extent measurement error for the remaining 50%, of the phenotypic variance (5,6,19). Our estimation of odds ratios implied that the influence of obesity (environment) was

about 1.5 times stronger than the influence of parental hypertension (heredity).

A polygenic heredity of hypertension has been suggested, with several possible genetic defects (10,19). Such hereditary mechanisms for hypertension could be independent of the mechanisms due to obesity. For instance, the blood pressure may have a genetically determined sensitivity to salt intake. Obese subjects often eat more daily salt than nonobese. Furthermore, it was recently shown that obesity in some way increases the salt-sensitivity (12). Then, obesity may acce ntuate a genetically increased salt-sensitivity, and increase the risk for hypertension. In the present study, the relative risk for hypertension was as high as 9 with both parental hypertension and obesity present.

In this study, as e.g. in Framingham (5,13), BP was recorded casually in a standardised setting. The possibility of misrecording of a hypertensive was mitigated by the fact, that 75% of the hypertensives were previously diagnosed. Another matter, use of the same cuff size in spite of different arm circumferences, could be excluded here. When eliminating all participants with RBMI >130% from the statistical analysis, the same strengths of significance were still obtained concerning odds ratios and F-values (not shown in Table).

Finally, we included a third predictor of BP, 2-h glucose (1), in the analyses. IGT was frequent among the hypertensives, 25%. Anti-hypertensive agents were present as often in hypertensives with IGT, as in those with normal glucose tolerance. We found that both parental hypertension, BMI and 2-h glucose were independent predictors of hypertension, implying separate causative influences by each predictor. Furthermore, parental hypertension was not interrelated to 2-h glucose or BMI, underlining the separate influence by genetic mechanisms. 2-h glucose and BMI were interrelated, however, implying that a hypertensive factor common to IGT and obesity may also exist, like hyperinsulinemia and insulin resistance (2,7,11).

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