Are racial differences in essential hypertension due to different pathogenetic mechanisms?

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Summary
1. Plasma noradrenaline concentration and plasma renin activity were measured in a control, British, urban population \( (n = 115) \) in which blacks were matched for age and sex with whites.
2. Similar measurements were made in subjects with essential hypertension (77 white and 23 black), and 48 healthy normotensive white civil servants.
3. In controls blood pressure was significantly higher in blacks; it correlated with age in both races and with pulse rate in blacks. There were no significant racial differences in plasma noradrenaline which was positively correlated with age in both blacks and whites. Mean plasma renin activity was 55% lower in blacks, and this difference was not related to urinary sodium excretion.
4. In hypertensive subjects plasma noradrenaline positively correlated with age in blacks. This relationship was not found in whites in whom 20% of young hypertensive subjects \(<45\) years had significantly raised plasma noradrenaline. Plasma renin activity was again significantly lower in blacks. In white hypertensives plasma noradrenaline and renin activity were significantly correlated.
5. There may be racial differences in the pathogenesis of essential hypertension.

Key words: essential hypertension, plasma noradrenaline, plasma renin activity, racial differences.

Abbreviation: PRA, plasma renin activity.

Introduction
Essential hypertension is common in urban negroes, it tends to be more severe in blacks than whites and is accompanied by greater morbidity and mortality (Stamler, Schoenberger, Shekelle & Stamler, 1974).

Essential hypertension may be accompanied by an increase in the activity of the sympathetic nervous system (Doyle & Smirk, 1955; Esler & Nestel, 1973), and features of sympathetic overactivity in mild essential hypertension associated with high PRA have been reported (Esler, Julius, Zweifler, Randall, Harburg, Gardiner & De Quattro, 1977). It has also been claimed that levels of PRA may have prognostic significance in patients with essential hypertension (Brunner & Laragh, 1973), although this point is disputed.

This study explores the possibility that racial differences in hypertension might be accompanied by differences in circulating catecholamines and PRA.

Subjects and methods

Study I
115 volunteer subjects were investigated. Black (West Indian or African) factory employees \( (n = 53) \) were matched for age and sex with whites \( (n = 62) \). Subjects attended a factory clinic between 07.00 and 09.30 hours. After sitting for 10 min blood pressure and pulse were recorded on three occasions (Bosomat automatic recorder), the lowest reading being used for subsequent analysis. A sample of blood was withdrawn by venepuncture for radioenzymic estimation of plasma noradrenaline and plasma renin activity.
noradrenaline (Henry, Starman, Johnson & Williams, 1975), and for radioimmunoassay of PRA (Boyd, Adamson, Fitz & Peart, 1969). A urine sample was obtained for estimation of sodium and creatinine.

Study 2

100 referred patients with untreated essential hypertension and normal renal function were studied. No cause for their hypertension had been discovered on investigation.

48 white control normotensive subjects were also studied (Sever, Osikowska, Birch & Tunbridge, 1977).

Subjects were investigated between 09.00 and 10.30 hours. Samples for noradrenaline and PRA were withdrawn from an indwelling venous cannula after recumbency for 1 h, and pulse and blood pressure were recorded. Observations were repeated after standing for 5 min and a further sample obtained for plasma noradrenaline. A 24 h urine collection was obtained for sodium and creatinine estimation.

Data were analysed on the CDC 6000 series computer at the University of London computer centre using the statistical Package for the Social Sciences (Nie, Hall, Jenkins, Steinbrenner & Bent, 1975). The significance of differences between correlation coefficients was tested using Fisher’s z-transformation. Plasma noradrenaline and PRA showed skewed distribution but log plasma noradrenaline and log PRA were more nearly normal in distribution and therefore used in calculating correlations and differences in means between groups. Results are reported mean ± 1 sd.

Results

Study 1

Blacks and whites were matched for age (white 43 ± 8 sd, black 43 ± 6) and reasonably well matched for sex (white male n = 37, female n = 25; black male n = 35, female n = 18). Blood pressure was significantly higher in blacks (132/93 ± 15/13) than whites (122/85 ± 14/9) (P < 0.001). It increased with age in both races and correlated significantly (P < 0.001) with pulse rate in blacks.

There were no significant racial differences in plasma noradrenaline (white: 461 ± 269 pg/ml; black: 452 ± 177 pg/ml) and log plasma noradrenaline correlated positively with age in both groups (white: r = 0.32, P < 0.05; black: r = 0.29, P < 0.05). PRA was lower in blacks (500 ± 537 pg h⁻¹ ml⁻¹) than in whites (1114 ± 781 pg h⁻¹ ml⁻¹) (P < 0.001) and this difference was not explained by differences in sodium status as urinary sodium concentration and urine sodium/creatinine ratios were very similar in both groups. In neither group

| Table 1. Blood pressure, pulse rate, plasma noradrenaline (NA) and PRA of normotensive controls and white and black hypertensive subjects |
|---|---|---|---|---|---|
|   | Control normotensive (C) | White hypertensive (WH) | Black* hypertensive (BH) |   |
| Number of subjects | 48 | 77 | 23 |   |
| Age (years) | 47 ± 9 | 45 ± 13 | 43 ± 12 |   |
| Blood pressure (mmHg) |   |   |   |   |
| Recumbent | 120/81 ± 12/9 | 158/100 ± 27/15 | 164/109 ± 23/12 | <0.001 | <0.05 |
| Standing | 121/86 ± 15/8 | 156/105 ± 27/16 | 163/115 ± 21/14 | <0.001 | <0.05 |
| Pulse (beats/min) |   |   |   |   |
| Recumbent | 72 ± 9 | 79 ± 13 | 67 ± 8 | <0.01 | <0.01 |
| Standing | 83 ± 13 | 91 ± 15 | 78 ± 16 | <0.01 | <0.01 |
| Plasma NA (pg/ml) |   |   |   |   |
| Recumbent | 413 ± 195 | 404 ± 222 | 378 ± 173 | <0.01 | <0.01 |
| Standing | 685 ± 249 | 747 ± 441 | 615 ± 292 | <0.01 | <0.01 |
| % Change in plasma NA on standing |   |   |   |   |
| Recumbent | 41% ± 55 | 98 ± 86 | 67 ± 44 | <0.01 | <0.01 |
| Standing |   |   |   |   |
| PRA (pg h⁻¹ ml⁻¹) |   |   |   |   |
| Recumbent | 791 ± 512 | 973 ± 1070 | 343 ± 561 | <0.01 | <0.001 |
| Renal excretion of Na⁺ (mmol/day) |   |   |   |   |
| — | 148 ± 60 | 164 ± 61 | — | <0.01 | <0.01 |

* Black = African or West Indian.
were plasma noradrenaline and PRA related. No sex differences in blood pressure, pulse, plasma noradrenaline, PRA or sodium excretion were found.

**Study 2**

Again normotensive controls and hypertensive subjects of both races were matched for age (Table 1). Blood pressure was significantly higher in black than white hypertensive subjects, but resting pulse was lower in the blacks.

Recumbent and standing plasma noradrenaline were similar in the three groups and significantly correlated with age in controls ($r = 0.47, P < 0.001$; $r = 0.52, P < 0.001$, respectively) and in black hypertensive subjects ($r = 0.63, P < 0.001$; $r = 0.65, P < 0.001$), but not in white hypertensive subjects ($r = 0.03, P = 0.8; r = 0.10, P = 0.4$).

Comparing these correlation coefficients shows that mean recumbent and standing plasma noradrenaline to age correlations in white hypertensive subjects differ significantly from controls ($P < 0.05$) and black hypertensive subjects ($P < 0.05$).

Among white hypertensive subjects significantly elevated plasma noradrenaline was evident in younger patients (<45 years), compared with age matched controls ($P < 0.01$): 20% of this group of hypertensive subjects were outside the 95% confidence limits for their age-matched controls. White hypertensive subjects showed a greater increment in plasma noradrenaline on standing than black hypertensive subjects.

PRA was lower in blacks. When the data for all white subjects in study 2 were pooled there was a significant correlation between log plasma noradrenaline and log PRA ($r = 0.27, P < 0.01$). This relationship achieved greater significance in white hypertensive subjects ($r = 0.41, P < 0.001$) and partial correlation coefficients between log plasma noradrenaline and log PRA controlling for age were also higher ($r = 0.48, P < 0.001$). No such relationship was observed in black patients. In neither study was there a significant correlation between plasma noradrenaline and blood pressure.

**Discussion**

The greater prevalence of high blood pressure in urban blacks compared with whites was confirmed in the first study.

Plasma noradrenaline concentration has been shown to be a useful determinant of sympathetic activity, (Lake, Zeigler & Kopin, 1976; Osikowska & Sever, 1976), but no differences were shown between the two racial groups in this 'normal' population. Plasma renin determinations, however, showed striking differences with low values commonly found in the blacks. It is not known to what extent genetic factors determine PRA values, but the observed differences cannot be accounted for by variations in sodium status.

Reported differences between plasma noradrenaline in essential hypertensive and normotensive subjects have been less clearly defined in recent studies, in which populations have been more carefully controlled (Sever, 1978).

In our second study, hypertensive subjects were evaluated according to age and race. The disposition of plasma noradrenaline was different in white hypertensive subjects compared with controls. The failure to demonstrate a correlation between plasma noradrenaline and age in this group suggested an inappropriate increase in plasma noradrenaline in younger patients, which may indicate sympathetic over-activity. The greater postural change in plasma noradrenaline in white hypertensive subjects would support this view. No such abnormalities occurred in black hypertensive subjects.

The relationship between plasma noradrenaline and PRA in white hypertensive subjects may be relevant. This inter-relationship supports the hypothesis that neurogenic factors are involved in the pathogenesis of high renin mild essential hypertension. In addition, neurogenic factors acting on the sympathetic nervous system and renin–angiotensin system may underline important racial differences in the pathogenesis and natural history of essential hypertension.

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**References**


