Physiological, Psychological, and Behavioral Factors and White Coat Hypertension

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Patients with hypertension in the clinic but not during daily activities ("white coat" hypertension) may be at lower risk of hypertensive morbidity and mortality than patients with hypertension in both settings ("persistent" hypertension). We hypothesized that the white coat phenomenon was due to greater blood pressure reactivity to the stress of a clinic visit and that, as a consequence, white coat hypertensive patients would display greater blood pressure reactivity to exercise and mental stress, as well as increased emotional reactivity and higher levels of anger, anxiety, or depression. We studied 89 patients with essential hypertension between 29 and 59 years old with ambulatory blood pressure monitoring, treadmill exercise testing with oxygen consumption measurement, mental stress testing (including mental arithmetic, public speaking, and video game tasks), and psychological testing (State-Trait Anxiety Scale, Cook-Medley Hostility Scale, Center for Epidemiologic Studies Depression Scale, emotional reactivity scale). We defined white coat hypertension as a mean ambulatory systolic blood pressure of 135 mm Hg or less and diastolic 85 mm Hg or less and persistent hypertension as a mean ambulatory systolic blood pressure of 140 mm Hg or more or diastolic 90 mm Hg or more. Forty-nine patients were classified as persistent hypertensives and 20 as white coat hypertensives. No significant differences were seen in demographic or clinical characteristics, fitness level, blood pressure response to exercise or mental stress, or psychological characteristics, except that white coat hypertensive patients had lower systolic blood pressures in the clinic and during exercise and greater variability of clinic diastolic blood pressures. Thus, we were unable to distinguish white coat from persistent hypertensive patients by these clinical, demographic, emotional, or reactivity measures. (Hypertension 1990;16:140–146)

As many as 21% of patients who have elevated blood pressure in the clinic have normal blood pressure on ambulatory blood pressure monitoring. This phenomenon, called office or "white coat" hypertension, is clinically significant because ambulatory blood pressure is a better predictor of morbidity and mortality from hypertension than is clinic blood pressure. Thus, patients with white coat hypertension, by virtue of their normal ambulatory blood pressures, may be at lower risk than patients in whom hypertension is present both in the clinic and on ambulatory monitoring ("persistent" hypertension). The reason for the white coat phenomenon is unclear.

We hypothesized that white coat hypertension occurs because some patients who are normotensive during everyday life respond to the stress of a clinic visit with a substantial increase in their blood pressure, thus making them appear hypertensive. Such patients might be expected to respond to other physical and mental stressors with greater blood pressure increases than do patients with persistent hypertension. Furthermore, we hypothesized that white coat hypertensive patients would be more likely than persistent hypertensive patients to experience such negative emotions as anxiety, hostility, and depression. To test these hypotheses, we exposed a persistent hypertensive and a white coat hypertensive group to a variety of physical and mental stressors and performed psychometric testing to assess personality traits and emotional characteristics that might distinguish these two groups of patients.

Methods

Subjects

Hypertensive patients were recruited from the community using newspaper, radio, and television advertisements, and from hospital outpatient clinics.
Patients were eligible if they were between 29 and 59 years old, weighed less than 120% of their ideal weight according to Metropolitan Life tables, had a history of essential hypertension, were not currently performing regular aerobic exercise, and had not taken antihypertensive medications within 6 weeks of being screened for the study. Patients were excluded if they had coronary artery disease or other organic heart disease, asthma, chronic obstructive pulmonary disease, or secondary hypertension. Informed consent was obtained from all subjects.

All patients had three blood pressures taken in a clinic setting by a nurse or research assistant 5 minutes apart on three separate occasions with a random zero sphygmomanometer. The fifth Korotkoff phase was used to indicate diastolic blood pressure. Patients were included if either their mean systolic blood pressure was between 140 mm Hg and 180 mm Hg or their mean diastolic blood pressure was between 90 mm Hg and 105 mm Hg, and if neither their systolic nor diastolic blood pressure were above the upper limits of 180 and 105, respectively. All patients underwent a physical examination by a physician to rule out secondary causes of hypertension and contraindications to exercise.

Body fat measurements were performed with skin calipers using a three-site technique. Then, on separate days, ambulatory blood pressure monitoring, exercise testing, mental stress testing, and psychological testing were performed.

**Ambulatory Monitoring**

Ambulatory blood pressure monitoring was performed using an Accutracker monitor (Suntech Medical Instruments, Raleigh, N.C.). Monitoring was done on a typical workday, and subjects were encouraged to pursue a variety of routine activities. Ambulatory monitors were placed on subjects at approximately 8:00 AM and were removed by subjects at bedtime. Recordings were not made during sleep. Blood pressures were recorded on a fixed schedule every 20 minutes. At each cuff inflation, subjects used a diary to record their posture (standing, sitting, lying), location (home, work, other), activities (physical activity, talking, eating, sleeping), use of caffeine, alcohol, or medications. In addition, using a five-point scale, subjects rated their mood along the following affective dimensions: bored/excited, peaceful/angry, pessimistic/optimistic, relaxed/tense, and sad/happy.

To test the calibration of the monitor, seven auscultatory and ambulatory monitor blood pressure measurements were performed simultaneously on a subset of subjects (n=35) using a Y-adapter. Ambulatory monitor blood pressures were on average 0.2/3.1 mm Hg below auscultatory blood pressures. When mean ambulatory blood pressure readings were adjusted for this calibration difference, classification as white coat or persistent hypertensive remained unchanged for 89% of subjects. In view of this high degree of agreement, unadjusted ambulatory blood pressures were used to classify subjects as white coat or persistent hypertensive patients.

An ambulatory monitoring session was considered acceptable if there were at least 25 usable blood pressure readings over a minimum of 8 hours. Four subjects were restudied because of an inadequate number of readings. Readings were considered artifactual and were rejected if the diastolic blood pressure was 40 mm Hg or less or 140 mm Hg or more, and systolic blood pressure was 90 mm Hg or less or 245 mm Hg or more, or pulse pressure was less than 20 mm Hg. In addition, readings were rejected if the monitor indicated that the electrocardiogram signal was inadequate, the Korotkoff sounds were faint or too few could be heard, or if the blood pressure reading during arm movement or a loose cuff was an extreme value (10 mm above or below the highest or lowest blood pressure reading without arm movement or a loose cuff). A mean of nine readings were rejected per subject.

**Exercise Testing**

Maximal treadmill exercise testing was performed using a modified Balke protocol. Graded exercise testing began at 2.0 mph and 0% grade. Grade and speed were systematically increased at the rate of 1 metabolic equivalent of the task (MET)/min (3.5 ml O₂ kg⁻¹ min⁻¹) with continuous electrocardiographic monitoring. Expired gases were collected for determination of peak oxygen consumption using a Beckman Metabolic Cart gas analyzer. Blood pressures were measured immediately before exercise, every 2 minutes during exercise, and at peak exercise.

**Mental Stress Testing**

Mental stress testing was performed in a sound attenuated, constant temperature chamber. Blood pressures were measured automatically with a Dinamap monitor (Critikon Corp., Tampa, Fla.). First, patients were asked to sit quietly for 40 minutes. Then, subjects performed a series of mental stress tasks as outlined in Table 1, with a rest period between each task to allow the blood pressure to return to baseline. For the mental arithmetic task, subjects were asked to add the digits of a three-digit number (e.g., 111=1+1+1=3); this sum was then...
added to the original three-digit number to form a new three-digit number (e.g., 111 + 3 = 114). Subjects then repeated this procedure for the new number. For the public speaking task, subjects were given a choice of controversial topics, and were asked to talk to an audience of three people after only 30 seconds of preparation. For the forehead ice pack task, an ice pack was applied to the forehead for 3 minutes. This has been shown to be a potent stimulant of the α-adrenergic system.6 Lastly, for the video game task, subjects played Demon Attack on an Atari computer.

Psychological Testing

Subjects were administered a battery of psychometric tests that included: 1) the Cook-Medley Hostility Scale,9 a 50-item true-false questionnaire that assesses the propensity to experience anger and hostility; 2) the State-Trait Anxiety Inventory,10 a 40-item questionnaire that measures anxiety at the time of the assessment (state anxiety) and the general tendency to experience anxiety (trait anxiety); 3) a nine-item emotional reactivity scale11 designed to assess the tendency to become emotionally aroused; and 4) the Center for Epidemiologic Studies Depression Scale,12 a 20-item scale that assesses how many days in the past week the subject experienced symptoms associated with depression. The emotional reactivity scale has been associated with systolic blood pressure elevations,11 and the Cook-Medley Hostility Scale has been associated with cardiovascular disease.13,14

Data Analysis

Subjects were defined as having white coat hypertension if both their mean ambulatory systolic blood pressure was 135 mm Hg or less and diastolic blood pressure was 85 mm Hg or less, values well within the normotensive range. Persistent hypertensive patients had systolic or diastolic hypertension on ambulatory blood pressure monitoring (mean ambulatory systolic blood pressure 140 mm Hg or more or diastolic blood pressure 90 mm Hg or more). All other subjects were classified as intermediate, and were not considered in the analyses.

For continuous variables, two-tailed t-tests were used to test for significant differences between means. For dichotomous variables, χ²-tests were used to test for significant differences. To test for an overall difference between persistent and white coat hypertensive patients in the level of blood pressure during mental stress testing, repeated-measures analysis of variance was used, with all rest periods and all four tasks included in the model. To test for differences between the two groups in the pattern of blood pressure response to individual tasks, separate repeated-measures analysis of variance models were performed for each task. Each model tested the blood pressure change from the preceding rest period to the task to the succeeding rest period. For all analyses, a p-value of 0.05 was considered significant. Power calculations were performed according to the method of Rosner.15

Analysis of diary entries during ambulatory blood pressure monitoring revealed strong associations between ambulatory blood pressure and posture at the time of measurement (standing, sitting, lying), location of the measurement (home, work, other), and the time of day of the blood pressure measurement. Consequently, we adjusted each subject’s mean ambulatory blood pressure for these three variables using regression techniques. All blood pressures were adjusted to the sitting position, at home, at the mean time of day that blood pressures were measured (2:49 PM). Subjects were then reclassified as white coat, persistent, or intermediate based on these adjusted blood pressures. The reclassification resulted in three of 20 (15%) white coat subjects becoming intermediate subjects, and one of 49 (2%) persistent subjects becoming an intermediate subject. When the analyses were repeated using the new subject classifications, no changes were seen in the results. Therefore, all results are presented with subject classification based on the unadjusted means.

Results

Of the 83 subjects who were eligible for this study, 49 (59%) were classified as persistent hypertensive, 20 (24%) as white coat hypertensive, and 14 (17%) as intermediate. Among the 69 study subjects, only 25 (36%) had ever been on antihypertensive medications, and of these 25 subjects, 15 (60%) had discontinued their medication at least 3 months before entry into the study. The persistent hypertensive group had a mean clinic blood pressure of 145/96 mm Hg and a mean ambulatory blood pressure of 148/91 mm Hg, whereas the white coat hypertensive group had a mean clinic blood pressure of 136/94 mm Hg and a mean ambulatory blood pressure of 128/80 mm Hg (Table 2). There was a significant difference between the two groups in clinic systolic blood pressure (p = 0.009) but not in clinic diastolic pressure (p = 0.62).

According to the diary entries, during ambulatory blood pressure monitoring there were no significant differences between the white coat hypertensive and the persistent hypertensive groups in alcohol or caffeine use, percentage of blood pressure measurements performed while talking or sleeping, use of drugs, and mood (bored/excited, peaceful/angry, pessimistic/optimistic, relaxed/tense, sad/happy).

There were no significant differences between the persistent hypertensive and the white coat hypertensive group in such demographic and clinical variables as age, race, sex, percent body fat, family history of hypertension, or duration of hypertension (Table 2).

Using the standard deviation of the mean blood pressure as an indicator of blood pressure variability, there were no significant differences between the persistent hypertensive and the white coat hypertensive groups in the variability of systolic or diastolic blood pressure during either clinic screening or ambulatory monitoring, except for a somewhat greater variability of clinic diastolic blood pressure in
the white coat hypertensive group (Table 3). In addition, when the differences between mean blood pressures at work and at home were computed for each subject, the white coat hypertensive and the persistent hypertensive groups did not differ.

Next, we examined blood pressure response to treadmill exercise testing. The persistent hypertensive and the white coat hypertensive groups showed similar levels of aerobic fitness, as reflected by their peak oxygen consumption (31.4±6.5 ml O₂ kg⁻¹ min⁻¹ versus 31.2±5.1 ml O₂ kg⁻¹ min⁻¹, p=0.88) and exercise duration (11.4±2.0 minutes versus 11.4±2.0 minutes). The persistent hypertensive group showed a greater systolic blood pressure at peak exercise than did the white coat hypertensive group (205±19 versus 184±21 mm Hg, p=0.0002) as well as a greater maximum systolic blood pressure during exercise (205±21 versus 185±19 mm Hg, p=0.001). However, no differences were found in systolic blood pressure reactivity to exercise (Table 4). No differences were observed in any of the measures of diastolic blood pressure (Table 4).

Psychological testing did not reveal any significant differences between the persistent hypertensive and the white coat hypertensive groups in depression, state or trait anxiety, emotional reactivity, or hostility (Figure 1).

Mental stress testing revealed consistently higher systolic and diastolic blood pressures in the persistent hypertensive group (systolic blood pressure, p=0.001; diastolic blood pressure, p=0.002) (Table 5, Figure 2). However, for each task, the pattern of blood pressure reactivity was similar for the white coat hypertensive and the persistent hypertensive groups. Heart rate response to the most challenging task, public speaking, was also analyzed. No difference was found in heart rate response between white coat and persistent hypertensive patients (p=0.79).

Discussion
Past studies have shown that clinic blood pressures tend to be higher than ambulatory blood pressures, and that clinic blood pressures taken by a physician tend to be higher than those taken by a nurse. A possible explanation for this phenomenon is that having blood pressure taken in a clinic setting is a stressful event for patients. Patients with a pronounced blood pressure response to clinic blood

<table>
<thead>
<tr>
<th>Variable</th>
<th>Persistent hypertension (mm Hg)</th>
<th>White coat hypertension (mm Hg)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinic SBP</td>
<td>7.1±3.0</td>
<td>7.8±4.1</td>
<td>0.44</td>
</tr>
<tr>
<td>Clinic DBP</td>
<td>4.3±1.8</td>
<td>5.6±2.5</td>
<td>0.02</td>
</tr>
<tr>
<td>Ambulatory SBP</td>
<td>11.3±2.6</td>
<td>11.1±2.3</td>
<td>0.79</td>
</tr>
<tr>
<td>Ambulatory DBP</td>
<td>9.6±2.1</td>
<td>9.0±2.2</td>
<td>0.28</td>
</tr>
<tr>
<td>Work SBP—home SBP</td>
<td>4.4±8.0</td>
<td>4.3±8.2</td>
<td>0.99</td>
</tr>
<tr>
<td>Work DBP—home DBP</td>
<td>4.6±5.3</td>
<td>5.5±8.2</td>
<td>0.61</td>
</tr>
</tbody>
</table>

Values for blood pressure are mean±SD. SBP, systolic blood pressure; DBP, diastolic blood pressure.
TABLE 4. Blood Pressure Response to Exercise

<table>
<thead>
<tr>
<th>Variable</th>
<th>Persistent hypertension (mm Hg)</th>
<th>White coat hypertension (mm Hg)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP at peak exercise</td>
<td>205±19.0</td>
<td>184±20.6</td>
<td>0.0002</td>
</tr>
<tr>
<td>DBP at peak exercise</td>
<td>94±10.2</td>
<td>90±9.9</td>
<td>0.27</td>
</tr>
<tr>
<td>Highest exercise SBP</td>
<td>205±20.9</td>
<td>185±19.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Highest exercise DBP</td>
<td>97±9.2</td>
<td>95±8.8</td>
<td>0.36</td>
</tr>
<tr>
<td>SBP reactivity</td>
<td>60±19.7</td>
<td>51±18.9</td>
<td>0.12</td>
</tr>
<tr>
<td>DBP reactivity</td>
<td>5±7.9</td>
<td>5±8.1</td>
<td>0.83</td>
</tr>
</tbody>
</table>

Values of blood pressure are mean±SD. SBP, systolic blood pressure; DBP, diastolic blood pressure; SBP reactivity, highest exercise SBP—mean resting SBP; DBP reactivity, highest exercise DBP—mean resting DBP.

Blood pressure measurement might appear hypertensive in the clinic but be normotensive during daily life. Our primary hypothesis was that these patients, so-called white coat hypertensives, would be distinguishable from persistent hypertensive patients in the laboratory setting by their enhanced blood pressure reactivity to mental and physical stressors. Secondly, we hypothesized that white coat hypertensive patients would show a greater tendency to experience depression, anxiety, and hostility.

However, after examining demographic, clinical, and psychological characteristics, as well as patterns of blood pressure response to mental stress and exercise, few differences were found between the white coat hypertensive and the persistent hypertensive groups. The white coat hypertensive group had lower systolic blood pressures in the clinic and during exercise, as well as lower systolic and diastolic blood pressures during all phases of mental stress testing. In addition, the white coat hypertensive group showed greater variability of clinical diastolic blood pressures. Otherwise, no significant differences were found between these two groups. Thus, white coat hypertension cannot be attributed simply to an increased blood pressure reactivity to the stress of blood pressure measurement in the clinic setting.

Anger, anxiety, and hostility are related to blood pressure reactivity to laboratory stressors. However, these factors were not associated with white coat hypertension in this study. Furthermore, the white coat hypertensive group did not score higher on the emotional reactivity scale, which measures the intensity of emotions that a person tends to experience in stressful situations. Emotional reactivity is associated with higher systolic blood pressures.

Pickering et al. found that the white coat hypertensive group tended to be female, younger, weigh less, and have a shorter duration of hypertension. These findings were not duplicated in the present study. Both Pickering et al. and the present study found little difference between the white coat hypertensive and the persistent hypertensive groups in blood pressure variability, as reflected in the standard deviation of ambulatory blood pressure and blood pressure reactivity to work. In addition, we found no difference in blood pressure or heart rate reactivity to laboratory-induced mental stress.

Floras et al. compared hypertensive patients whose office blood pressure was at least 10 mm Hg above ambulatory blood pressure to patients whose office blood pressure was less than 10 mm Hg above ambulatory blood pressure. They found that there was no difference between these two groups in variability of ambulatory blood pressure (as measured by

TABLE 5. Blood Pressure Response to Mental Stress

<table>
<thead>
<tr>
<th>Task</th>
<th>Persistent hypertension (mm Hg)</th>
<th>White coat hypertension (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>138±11/88±9*</td>
<td>127±9/82±6</td>
</tr>
<tr>
<td>Mental arithmetic</td>
<td>159±16/99±9</td>
<td>149±15/94±8</td>
</tr>
<tr>
<td>Rest</td>
<td>145±12/90±8</td>
<td>131±8/85±6</td>
</tr>
<tr>
<td>Public speaking</td>
<td>175±13/111±9</td>
<td>160±12/102±8</td>
</tr>
<tr>
<td>Rest</td>
<td>148±11/92±8</td>
<td>134±9/87±9</td>
</tr>
<tr>
<td>Forehead icepack</td>
<td>159±12/101±11</td>
<td>147±11/96±8</td>
</tr>
<tr>
<td>Rest</td>
<td>147±10/92±8</td>
<td>135±9/86±8</td>
</tr>
<tr>
<td>Video game</td>
<td>163±13/103±9</td>
<td>152±10/98±9</td>
</tr>
<tr>
<td>Recovery</td>
<td>145±10/93±8</td>
<td>133±8/86±7</td>
</tr>
</tbody>
</table>

Values are mean systemic blood pressure±SD/mean diastolic blood pressure±SD.
the standard deviation) or in blood pressure response to mental arithmetic. These findings are consistent with the present study. However, in contrast to the present study, Floras et al\(^3\) did find greater blood pressure reactivity to exercise in the group with the greater difference in blood pressure between clinic and ambulatory settings. The two patient groups defined by Floras et al\(^3\) are not strictly comparable to the two groups defined in the present study, which may account in part for the discrepant findings.

Schneider et al\(^1\) divided subjects with clinic hypertension into two groups based on whether self-measured home blood pressures were elevated or normal. These two groups were analogous to the persistent and white coat groups defined in the present study. Consistent with the present study, Schneider et al\(^1\) found no difference between the two groups in anger or anxiety, as measured by the State-Trait Personality Inventory.

Adequate power was available to find clinically significant differences in most of the variables of interest. Over 90% power was present to find an age difference of at least 7.5 years between the white coat and persistent hypertensive group, a 15% or greater difference in percentage body fat, and a 10 mm Hg or greater difference in diastolic blood pressure reactivity to exercise. Over 80% power was present to find at least a 4-year difference in length of hypertension, a 15% or greater difference in maximum oxygen consumption, and a 15 mm Hg or greater difference in systolic blood pressure reactivity to exercise. There was 78% power to find a 25% greater percentage of men in the persistent hypertensive group. Because of a relatively small number of nonwhite subjects, power was inadequate to detect differences in race.

A potential limitation of this study concerns whether, in categorizing subjects as white coat hypertensive, we were simply selecting for those patients with milder hypertension. Although the white coat hypertensive group had lower systolic blood pressures than did the persistent hypertensive group, their diastolic blood pressures were not significantly different. Because both systolic and diastolic blood pressure criteria had to be met when subjects were defined as white coat or persistent hypertensives, any tendency to label subjects with lower clinic systolic blood pressures as white coat would mainly affect those subjects with isolated systolic hypertension. Only seven subjects (11%) had isolated systolic hypertension; the others had either isolated diastolic hypertension \((n=28, 41\%)\) or both systolic and diastolic hypertension \((n=34, 49\%)\). Thus, only a small number of subjects might have been mislabeled because of any tendency to classify those patients with milder systolic hypertension as white coat hypertensives.

The possibility of mislabeling milder hypertensive patients as white coat is present in other studies. Pickering et al\(^1\) defined white coat hypertension as being present when the office diastolic blood pressure was 90–104 mm Hg and the awake ambulatory blood pressure was less than 134/90 mm Hg. These authors found that white coat hypertensive patients, when compared with patients with sustained hypertension, had significantly lower clinic systolic blood pressures but nearly identical diastolic blood pressures, (white coat, 146/96 mm Hg; sustained, 154/98 mm Hg; \(p=0.001\) for systolic blood pressure, \(p=NS\) for diastolic blood pressure). These results are similar to our findings.

The results of this study and of the study by Pickering et al\(^1\) suggest that blood pressure differences between the white coat hypertensive and the persistent hypertensive group are not simply because of differences in blood pressure reactivity to stress. It has been suggested that the white coat phenomenon may be a classically conditioned response to the stimulus of a clinic visit.\(^1\) A careful examination of doctor-patient interactions might help reveal whether such conditioning occurs. If it is true that the white coat phenomenon is as common as studies suggest and that white coat hypertension is not associated with the same degree of morbidity and mortality as is persistent hypertension, then it clearly is of considerable clinical importance to understand why this phenomenon occurs, how to distinguish between patients with white coat and persistent hypertension in the most cost-effective manner, and how to clinically manage these patients.

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References


**KEY WORDS** • essential hypertension • ambulatory blood pressure monitoring • exercise tests • mental stress tests • psychological tests • white coat phenomenon
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