Cardiovascular Reactivity to Stress Predicts Future Blood Pressure Status

Karen A. Matthews, Karen L. Woodall, Michael T. Allen

Cardiovascular reactivity to stress may have a pathophysiological role in neurogenic hypertension. We studied the value of measuring blood pressure change during standardized mental and physical challenges to prediction of resting blood pressure status 6.5 years later among 206 middle-aged adults and their 164 children, with the latter group originally being tested while enrolled in elementary through high school. After adjustment for age, resting blood pressure, and body mass index at study entry, as well as length of follow-up, larger systolic and diastolic blood pressure responses to a combination of mental and physical challenges were associated with higher subsequent resting diastolic blood pressure 6.5 years later among adults. Among boys, but not among girls, larger systolic and diastolic blood pressure responses to challenge were associated with higher subsequent resting blood pressure. These data suggest that people who are at high risk for elevated blood pressure might have an exaggerated stress-induced cardiovascular response at a younger age. (Hypertension. 1993;22:479-485.)

KEY WORDS • stress • blood pressure • prospective studies • isometric contraction

Excessive cardiovascular reactivity to stress may have a pathophysiological role in neurogenic hypertension. Although controversial, this hypothesis has been evaluated by only a few prospective studies. Six studies have used the cold pressor test, and only two report that blood pressure reactivity to the cold pressor test is related to subsequent hypertensive status. The choice of the cold pressor test to elicit cardiovascular reactivity in these studies might not have been optimal, however. This is because, relative to normotensive individuals, borderline hypertensive subjects do not exhibit larger blood pressure responses to the cold pressor test in the majority of studies, whereas they do exhibit larger blood pressure and heart (HR) rate responses during psychological challenges requiring an active behavioral response, eg, mental arithmetic. The cold pressor test also does not elicit a β-adrenergically mediated myocardial response, which is thought to be important to early neurogenic hypertension.

At least three longitudinal studies of the reactivity hypothesis have used psychological challenges requiring an active behavioral response. Light et al reported that systolic blood pressure (SBP) and HR responses to a reaction time task by 30 undergraduate men were related to subsequent blood pressure status 10 to 15 years later. These men were drawn from an original sample of 208 male undergraduates. Borghi et al found that among 44 borderline hypertensive subjects, those who subsequently developed sustained hypertension in the next 5 years had initially demonstrated high diastolic reactivity to a mental arithmetic task and had high sodium levels. These studies, although important, are not definitive because of their small sample sizes, low or unknown percentage of individuals retrieved for follow-up, and the unique nature of the initial samples.

More recent study of 292 white and 46 black children, initially enrolled in third grade, does not have these design difficulties. Murphy et al reported that SBP reactivity to a video game was related to subsequent resting SBP levels 4 years later among white and black children, whereas diastolic blood pressure (DBP) reactivity to a video game was related to subsequent DBP in the black children only. Results were not analyzed according to sex of the children.

We report here the results of a prospective analysis of the relation between cardiovascular reactivity to mental and physical challenges, other than the cold pressor test, and subsequent blood pressure status in a large sample of adults and children followed for approximately 6.5 years. Analyses took into account the effects of age, weight, and other important risk factors for elevated blood pressure, and relationships were analyzed according to type of challenge and sex of participant.

Study Population

From 1983 through 1984, we measured cardiovascular responses to three standardized challenges among 260 adults and their 217 children from 142 families residing in a single suburban school district near Pittsburgh, Pa. At that time, the children were enrolled in elementary through high school. Almost 90% of these participating families were classified as upper middle class, with parents having at least some college education; and all were white or Asian. Except for 11 adults and 8 children who could not be traced and 1 adult who had died, all participants were invited for reevaluation.
of blood pressure, weight, height, and medical history on average 6.5 years later. Those agreeing to participate in the follow-up represented 83.2% (n=206) of the parents and 78.5% (n=164) of the children from this contacted group. Participation rates varied by whether or not the participants still resided within the Pittsburgh area. Those who still resided within 75 miles of Pittsburgh (n=181 parents and 122 offspring) had an 87.3% participation rate, whereas those who had moved out of state (along with three families who lived in Pennsylvania at least 75 miles away from the testing site) had a 61.6% participation rate.

Measurement of Blood Pressure and Heart Rate

SBP, DBP, and HR were measured for all subjects from 1983 through 1984 by an automated, digital electroxyphgmomanometer (IBS model SD-700A) on the nondominant arm. This is a portable, self-contained device that uses a low-frequency sensor mounted in the occluding cuff to detect arterial wall motion and Korotkoff vibrations. HR is determined simultaneously from oscillometric pressure surges. This device has automatic deflation, and the deflation rate can be adjusted for the varying HR among different age groups to increase the accuracy of blood pressure measurement. The device also indicates invalid readings due to movement, noise, inadequate inflation, etc. Pediatric, adult, and obese cuffs were used as appropriate to the arm size of the subject.

This device was interfaced with a Baumanometer mercury column to permit manual resting blood pressure readings simultaneous with the automated measures. All experimenters had received the training program for blood pressure assessment developed for the Multiple Risk Factor Intervention Trial and had passed the certification tests. In the original study sample, Pearson correlation coefficients between the IBS and manual resting SBP readings for fathers, mothers, sons, and daughters ranged from .94 to .99, with a mean difference of 0.81 mm Hg (SD=2.9). The comparable Pearson correlation coefficients for resting DBP (fifth-phase Baumanometer) were .90 to .96, with a mean difference of 0.77 mm Hg (SD=2.8).

This same method was used for measurement of blood pressure and HR at follow-up testing for participants continuing to live near Pittsburgh. Pearson correlation coefficients between automated and manual SBP readings for fathers, mothers, sons, and daughters at follow-up testing ranged from .89 to .97, with a mean difference of 2.41 mm Hg (SD=2.64). Comparable Pearson correlation coefficients between the two methods of DBP assessment were .86 to .92, with a mean difference of 3.16 mm Hg (SD=3.38).

Participants (14 men, 20 women, 12 boys, and 19 girls) living outside commuting distance at follow-up or who could not arrange to attend a testing session consented to their physicians’ providing their blood pressure, weight, and height most recently measured in the past year. Results of analyses conducted without these physician-tested participants were essentially the same as those results including all participants. Therefore, results below are presented for the full sample.

Procedures

The two testing sessions took place approximately 6.5 years apart (SD=0.46 years; range, 5.2 to 7.7 years) and both took place at a school in the families’ home school district. All participants provided informed consent to the procedures, and parents also provided written consent for the participation of their children at initial testing and at follow-up for children younger than 18. Procedures were reviewed and approved according to Institutional Review Board guidelines. At the first testing session, participants squeezed a hand dynamometer twice, separated by 15 seconds, to ascertain their maximal grip strength. Next, their arm circumference was measured, and the appropriately sized blood pressure cuff was attached with the microphone placed over the palpated brachial artery. An initial blood pressure reading was taken to check for correct placement of the cuff. Participants then relaxed for 10 minutes while listening to soothing, audiotaped environmental sounds through headphones and while their blood pressure and HR were measured at 30, 270, and 510 seconds. Automated and manual measurements of blood pressure were made simultaneously at the latter two times.

Participants were asked to complete three tasks with 3-minute rest periods between tasks. The order of the first two of these tasks—serial subtraction and mirror-image tracing—was counterbalanced. The third task— isometric handgrip exercise—was always presented last because blood pressure recovery time after this task can be prolonged. These tasks were selected because it had been demonstrated previously that they could be administered to different age and sex groups and elicited different patterns of cardiovascular responses.\textsuperscript{14,15}

In the serial subtraction task, participants were instructed to mentally and sequentially subtract backward by a given number aloud as quickly and accurately as possible for two 60-second periods. Parents and high school students were asked to subtract 13s from a four-digit number; middle school students (grades 6 through 8), 5s and then 7s from a three-digit number; and elementary school students, 2s and then 3s from a two-digit number.

In the mirror-image tracing task, participants were asked to trace with a metal stylus the outline of a star as quickly and accurately as possible for a 3-minute period. The challenging aspect of this task was that the star could be viewed only indirectly, as reflected in a mirror. The star-tracing apparatus was interfaced with a computer that beeped and recorded whenever the stylus was not on the star outline.

The isometric exercise task required participants to grip for a 2.5-minute period a hand dynamometer at 30% of the mean of their two maximal voluntary contractions measured at the beginning of the session. The hand dynamometer was interfaced with the computer, which beeped and instructed the subject to squeeze harder whenever the subject’s effort fell below the 30% maximal level. To avoid alterations in respiration patterns, participants were instructed to count softly during this task. They then completed health history and personality questionnaires and an interview for approximately 30 minutes. Participants then relaxed for an additional 10-minute period, again listening to soothing environmental sounds, while their blood pres-
sure and HR were recorded at 30, 270, and 510 seconds. Mercury column readings were also obtained at the time of the last two readings by the IBS. Finally, height and weight were measured.

At the follow-up testing, for participants within commuting distance, participants were seated while the study protocol was explained and consent forms were signed. Then they relaxed for 10 minutes without talking while their blood pressure and HR were measured at 30, 270, and 510 seconds. They completed demographic, health history, and personality questionnaires during this period but were instructed not to move their arms when the blood pressure cuff began to inflate. Afterward, their height and weight were measured. Consenting adults not living near Pittsburgh were mailed questionnaires and a form giving consent to contact their family physician to obtain a blood pressure, height, and weight measurement within the last year.

Data Reduction and Statistical Analysis

Of those tested at both sessions, 8 adults (4 women and 4 men) at the initial assessment and another 11 adults (8 men and 3 women) at the follow-up assessment reported taking prescription medications to lower blood pressure. These subjects were excluded from the primary analyses. Another 16 participants (4 men, 1 woman, 7 boys, and 4 girls) were excluded from analyses because their physician-reported blood pressure readings were dated more than 1 year from the time of the follow-up; ie, they did not meet study criterion for recency of blood pressure assessment. Thus, the final sample for whom data are presented in this report included 76 men, 106 women, 65 boys, and 88 girls.

All blood pressure measures taken during the first session tasks were averaged within each task separately. The last two readings (minutes 6 and 8.5) were also averaged across the postexperimental baseline rest period of the initial session and across the rest period of the follow-up session. These constituted the baseline readings, rather than the more usual use of preexperimental baseline rest periods. Session 1 postexperimental baseline readings of SBP, DBP, and HR were used because the postexperimental rest period was viewed as conceptually more comparable to the follow-up blood pressure assessment when subjects were not anticipating task performance demands. In addition, formal t tests showed that boys' and girls' postexperimental SBP resting levels were significantly lower than preexperimental SBP resting levels for boys and girls (P<.001), whereas adults did not differ in preexperimental versus postexperimental resting SBP levels. Relative to preexperimental DBP levels, postexperimental DBP resting levels were approximately 1 mm Hg higher for boys and women (P<.04) and were similar for girls and men.

Task-induced changes in SBP and DBP at session 1 were calculated as the difference between final rest period and average task level means; these change scores were then standardized within groups of adults and children separately for each task. Overall measures of SBP and DBP reactivity to stress were defined as the sum of comparable standardized change scores across the three tasks.

To evaluate the changes in resting blood pressure levels across the follow-up period, we used repeated-measures analysis of variance, and Pearson correlation or partial correlation coefficients assessed the extent of associations across time. To assess whether the associations between cardiovascular reactivity during tasks and subsequent blood pressure status were independent of potential confounders or risk factors for hypertension, we conducted partial correlations between the session 1 standardized reactivity measure (SBP or DBP) and session 2 blood pressure levels of adults and children separately, with the appropriate session 1 baseline measure, age, body mass index (BMI); sex; and length of time in months between assessments as covariates. Preliminary multiple regression models tested for the interactions of the standardized reactivity measure with session 1 age and BMI, length of follow-up, and sex. The only significant interaction effect between reactivity and these variables was found for sex with reactivity scores among children; as a consequence,
TABLE 2. Pearson Correlation Coefficients of Blood Pressure Across 6.5 Years

<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>Men</th>
<th>Women</th>
<th>Boys</th>
<th>Girls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>.64</td>
<td>.45</td>
<td>.48</td>
<td>.33</td>
</tr>
<tr>
<td>Diastolic</td>
<td>.43</td>
<td>.44</td>
<td>.09</td>
<td>.25</td>
</tr>
</tbody>
</table>

All correlations are significant, P<.05, except for r=.09.

subsequent partial correlations were conducted separately by sex to explicate these effects, and these results are described below. In all analyses, two-tailed probability values at less than .05 were considered to be significant.

Preliminary analyses comparing the characteristics of participants and nonparticipants showed that participating adults did not significantly differ from adults in the original sample who were not retested on the dependent measures from the original assessment, whereas participating children did differ from nonparticipating children on several measures from session 1. Relative to nonparticipating boys, participating boys had higher levels of session 1 resting DBP levels and a smaller increase from baseline to task levels in DBP and SBP (both P<.05). Participating relative to nonparticipating girls had a smaller session 1 change in DBP from baseline to mental arithmetic task level.

Results

Changes in and Stability of Blood Pressure Levels Across 6.5 Years

SBP levels (except among girls) and DBP levels (except among men) significantly increased over 6.5 years (Table 1). The association of SBP levels across time was moderate to substantial for all participants (Table 2), as was the association for adults' DBP levels. In contrast, a modest correlation between girls' DBP levels and a null correlation between boys' DBP levels occurred across the two sessions. Perhaps the correlation for DBP across time in children was lower than that for adults because of children's substantial changes in body size and composition between the two sessions. Boys' body weight increased an average of 24.5 (±12.9) kg between sessions, and girls' body weight gain across the same period averaged 13.2 (±9.5) kg.

Relation Between Cardiovascular Reactivity and Blood Pressure Status

Partial correlations showed that among adults, those who had greater challenge-induced SBP and DBP changes had greater DBP levels 6.5 years later, adjusted for initial resting DBP level, age, and BMI at study entry; sex; and duration of follow-up (Table 3). Analyses for men and women separately showed that this pattern tended to be reliable for men, whereas the association between DBP change (but not SBP change) during challenge and subsequent DBP levels was reliable for women. Adults' SBP status at follow-up was not predicted by cardiovascular reactivity measures. For

TABLE 3. Partial Correlations Between Combined Cardiovascular Reactivity Measures at Study Entry and Follow-up Blood Pressure Levels

<table>
<thead>
<tr>
<th>Study Entry Combined Task Measure</th>
<th>Follow-up</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td>Male Only</td>
<td>Female Only</td>
<td></td>
</tr>
<tr>
<td></td>
<td>SBP</td>
<td>DBP</td>
<td>SBP</td>
<td>DBP</td>
</tr>
<tr>
<td>Adults</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>168</td>
<td>.12</td>
<td>.05</td>
<td>.14*</td>
</tr>
<tr>
<td>SBP pressure reactivity</td>
<td>.166</td>
<td>.17†</td>
<td>.23‡</td>
<td>.25†</td>
</tr>
<tr>
<td>DBP pressure reactivity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>152</td>
<td>.14*</td>
<td>.25†</td>
<td>.09</td>
</tr>
<tr>
<td>SBP pressure reactivity</td>
<td>.151</td>
<td>.00</td>
<td>.35‡</td>
<td>.01</td>
</tr>
<tr>
<td>DBP pressure reactivity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SBP indicates systolic blood pressure; and DBP, diastolic blood pressure. Combined cardiovascular reactivity measures are task minus baseline change scores standardized for each task within age/sex groups and summed. Correlations were adjusted for resting blood pressure, age, and body mass index at study entry as well as length of follow-up.

*P<.10, †P<.05, ‡P<.01.
DBP (mm Hg)
81.00
79.00
77.00
75.00
1 2 3 4
QUARTILE

FIG 2. Bar graph shows mean diastolic blood pressure (DBP) at 6.5-year follow-up, adjusted for initial DBP, of adults classified into quartiles of the distribution of standardized DBP responses to combined mental and physical challenges.

SBP (mm Hg)
130.0
128.0
126.0
124.0
122.0
120.0
1 2 3 4
QUARTILE

FIG 4. Bar graph shows mean systolic blood pressure (SBP) at 6.5-year follow-up, adjusted for initial SBP, of boys classified into quartiles of the distribution of standardized SBP responses to combined mental and physical challenges.

illustration only, Figs 1 and 2 show the mean DBP levels at follow-up, adjusted for initial DBP levels, in individuals who were in each quartile of the distributions of standardized SBP and DBP reactivity scores at study entry.

Among children (Table 3), the greater the challenge-induced changes in SBP and DBP, the higher the resting SBP tended to be at follow-up, adjusted for initial resting blood pressure, age, and BMI at study entry; sex; and duration of follow-up. Similarly, the greater the DBP change to challenge, the higher the subsequent resting DBP tended to be at follow-up, adjusted for the covariates. Analyses conducted separately by sex showed that the overall pattern was due to the boys. For illustration only, Figs 3 through 5 show the mean SBP and DBP at follow-up, adjusted for resting initial SBP and DBP, respectively, in boys who were in each quartile of the distributions of reactivity at study entry.

Reactivity Based on Mental Versus Physical Stress and Blood Pressure Status

We next evaluated whether mental and/or physical challenge-induced measures of cardiovascular reactivity were predictors of subsequent blood pressure status 6.5 years later for those associations that were significant above. Among adults, DBP change in response to serial subtraction and star tracing at study entry was related to follow-up DBP, as was SBP change in response to serial subtraction, partialing out the corresponding entry level blood pressure, age, and BMI at study entry; length of follow-up; and sex (Table 4). Partial correlational analyses showed that even when statistically controlling for DBP responses to isometric exercise along with all the above covariates, the DBP change to serial subtraction ($P<.002$) and mirror-image tracing ($P<.03$) independently predicted DBP status 6.5 years later.

Adults' SBP change in response to serial subtraction tended to predict subsequent SBP status ($P<.07$), after controlling for SBP change during isometric exercise and the other covariates.

Boys' SBP responses to serial subtraction at study entry were related to their subsequent SBP status, adjusting for initial pressure, BMI, and age at study entry as well as length of follow-up, whereas their DBP responses to serial subtraction and star tracing were related to subsequent DBP status. The latter was true even when statistical controls were introduced for isometric exercise ($P<.03$ for serial subtraction and $P<.005$ for star tracing), and SBP responses to serial subtraction remained a significant predictor of future
SBP status, when statistical controls were introduced for isometric exercise responses as well as the other covariates \(P<.04\).

In only one case did blood pressure responses to isometric exercise predict subsequent blood pressure status, after adjustment for responses to the psychological challenges: men’s SBP responses to isometric exercise were significantly associated with subsequent DBP status. Thus, it appears that mental stress–induced blood pressure changes are related to subsequent blood pressure status, with physical stress–induced blood pressure change related in men only (Table 4).

**Hypertensive Versus Nonhypertensive Group Differences**

We explored whether the eight men and three women who began taking antihypertensive medications between study entry and follow-up testing could be distinguished on the basis of study entry measures from those adults who remained normotensive (follow-up blood pressure less than 140/90 mm Hg and not taking antihypertensive medications). As seen in Table 5, adults who developed hypertension had higher casual SBP and DBP levels and higher BMI at study entry than those adults who did not develop hypertension over the course of the study. Standardized SBP and DBP reactivity measures at study entry were higher among the newly diagnosed hypertensive subjects than among the normotensive subjects, but these differences did not achieve statistical significance.

**Discussion**

The present study confirmed that elevated blood pressure responses to a combination of mental and physical challenges were related to resting blood pressure status on average 6.5 years later among middle-aged adults and male children. Specifically, among adults, those who exhibited larger changes in SBP and DBP during challenges had a higher DBP level 6.5 years later. Male children who exhibited larger task-induced changes in DBP had higher follow-up SBP and DBP, whereas boys who exhibited larger task-induced changes in SBP had higher subsequent SBP. Furthermore, these relations were apparent even when statistical controls were introduced for age, BMI, and resting blood pressure at study entry as well as length of follow-up. Thus, the present associations between cardiovascular reactivity and blood pressure rise over time cannot be accounted for by those variables known to predict a rise in blood pressure. This study is first to report an association between future blood pressure status and cardiovascular reactivity to challenges other than the cold pressor test in a large sample of adults.

The present study also examined whether mental or physical challenge or both predicted rises in blood pressure. Although the analyses we conducted were not definitive, it did appear that more evidence supported the importance of mental stress–induced blood pressure changes than that of physical stress–induced blood pressure changes—a pattern anticipated on the basis of psychophysiological comparisons of borderline hypertensive and normotensive control individuals. Recall that borderline hypertensive subjects exhibited larger blood pressure changes during mental stress than did control subjects, whereas they did not exhibit larger blood pressure changes to the cold pressor test in the majority of studies. Thus, it may be that mental stress–
induced blood pressure changes provide a unique marker of future risk of hypertension.

Although not a major focus of the study, it is noteworthy that the relative SBP levels of the children were quite reliable across the follow-up period, when the children were experiencing large changes in weight and height and had experienced changes in levels of reproductive hormones. In a sample of 1501 children, correlations between the means of six blood pressure measurements taken at study entry and again 8 years later were 0.41 and 0.35 for SBP and DBP, respectively. In another sample of more than 4000 children, correlations between the means of three blood pressure measurements taken at study entry and again 6 years later were 0.31 and 0.18 for SBP and DBP, respectively. Thus, our correlations between the means of two SBP measures taken at study entry and again 6.5 years later of 0.48 and 0.33 for boys and girls, respectively, are quite comparable to those of other studies.

**Study Limitations**

We did not have a sufficient sample of adults who became hypertensive over the course of the follow-up period to permit definitive analyses of the utility of cardiovascular reactivity measures for prediction of essential hypertension. We did not have measures of parental history of hypertension for the adults at study entry, so we could not evaluate the extent to which this factor interacted with stress reactivity in predicting blood pressure rise over time. The sample was primarily white and largely upper middle class, and it is unknown whether the challenges we used or the cardiovascular responses to those challenges would have the same meaning in other samples at high risk for hypertension. For example, blacks may have different mechanisms accounting for their hypertension relative to whites and appear to respond differently during standardized challenges than whites. The measures of cardiovascular reactivity among girls were unrelated to rises in blood pressure over time. The null relation may be due to the small rise that this group experienced in blood pressure. Also, the null relation may be due to the fact that in a sample of children and adolescents, some of whom were in the present follow-up, blood pressure responses during stress declined or stayed the same in girls across 4 years, whereas they increased in boys. Thus, prepubertal assessment of girls' reactivity to stress may not accurately estimate the risk associated with that exposure over time.

The present study does not and cannot elucidate why short-term changes in blood pressure during stress are related to subsequent rises in blood pressure. Cardiovascular reactivity may represent one pathogenic mechanism in the development of high blood pressure; it may be a marker for a central defect in the autonomic control of the cardiovascular system; or it may reflect early changes in arterial compliance. Future longitudinal and clinical research is needed to disentangle the underlying mechanisms for the association of blood pressure reactivity to challenge and subsequent elevated blood pressure.

In sum, the present study suggests that blood pressure reactivity to combined mental and physical challenges may be an important marker of future blood pressure status. This marker appears to be important, independent of initial blood pressure levels, age, and BMI; length of follow-up; and for adults, sex.

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