Forearm Blood Flow Responses of Offspring of Hypertensives to an Extended Stress Task

Blaine Ditto and Sydney B. Miller

The forearm blood flow and other cardiovascular responses of 10 healthy young men with a parental history of hypertension to an extended laboratory stressor were compared with the responses of 10 age-matched men with normotensive parents. To eliminate the effects of the anticipation of stress on baseline measures, all subjects participated in a separate 1-hour counterbalanced baseline session in which no stress was presented. There were no significant differences between the two groups in resting blood pressure, heart rate, blood volume pulse, forearm blood flow and vascular resistance, and self-report anxiety, although offspring of hypertensive parents exhibited marginally greater (p=0.08) forearm blood flow at rest. During the stress session, subjects played video games for 1 hour and avoided mild electric shocks depending on performance. Offspring of hypertensive parents exhibited significantly greater heart rate (+19±6 vs. +3±2%), forearm blood flow (+52±14 vs. +9±4%), and self-report anxiety (+25±6 vs. +9±3%) responses to the task. There were no significant group differences in blood pressure response to the task. Significant positive correlations between forearm blood flow and heart rate responses to the task were observed. These findings extend earlier results that suggested healthy young offspring of hypertensive and normotensive parents may exhibit different patterns of hemodynamic response to stress in the absence of differences in resting blood pressure or blood pressure responsiveness to stress. (Hypertension 1989;13:181-187)

The role of psychological stress in the development of hypertension is an intriguing question but difficult to study. In the epidemiological literature, psychological stress has been operationalized as a demanding occupation,1 migration,2 and living in a poor, high crime3 or crowded4 environment. To some degree, evidence consistent with the notion that repeated or chronic psychological stress may be associated with an elevation of resting blood pressure can be found in each case. However, the relations between stress and blood pressure are typically weak, producing skepticism among many investigators concerning the importance of this potential risk factor. A stronger case for the importance of psychological stress as a risk factor for hypertension can be made if it is assumed that its effects are limited primarily to those who are in some manner psychologically or biologically susceptible.3 In recent years, considerable attention has been directed toward family history of hypertension and its possible interactions with psychological stress. Family history of hypertension is a well-documented risk factor for the disorder,9,10 and the results of a number of studies indicate a positive association between family history and cardiovascular response to stress, although the stressors employed in these studies are typically of 5-10 minutes' duration.11-15 It is not clear whether the responsiveness of individuals with a family history of hypertension to acute stress is reflected in their responsiveness to stress of longer duration, but an evaluation of the patterns of cardiovascular response to stress exhibited by normotensive individuals with a family history of hypertension would seem to be important. In a longitudinal study of children with a family history of hypertension, Falkner et al16 found blood pressure response to a 10-minute psychological stressor predicted the development of hypertension.

As Anderson et al15 note, most studies comparing the cardiovascular responses to stress of individuals with and without a family history of hypertension
have focused on the blood pressure and heart rate responses of these two groups. Relatively little information concerning the hemodynamic mechanisms of elevated blood pressure responsiveness is available. Regional blood flow has seldom been examined, and only Anderson et al have studied forearm blood flow responses to stress in individuals differing in familial risk. They found that adolescent offspring of persons with hypertension exhibited significantly greater increases in forearm blood flow to a 9-minute mental arithmetic task than offspring of normotensive persons. There were no group differences in resting blood pressure or blood pressure responsiveness to stress. These observations may be important for a number of reasons. For example, differences in regional blood flow responses to stress have been found between spontaneously hypertensive and Wistar-Kyoto rats that may appear in the absence of group differences in blood pressure responsiveness. Further, changes in regional blood flow over time, especially in the skeletal muscles, seem to be particularly important features of the cardiovascular responses of experimental animals and humans to sustained stress. Exaggerated blood flow responsiveness could be a precursor of an autoregulatory response or structural change.

The present investigation attempted to replicate and extend the findings of Anderson et al in two directions. First, the relations between heart rate, blood pressure, blood volume pulse, and forearm blood flow changes in healthy young adult offspring of hypertensive and normotensive parents were examined to obtain a clearer picture of the relations between regional blood flow and other cardiovascular changes during stress in these two groups. Second, the patterns of response of these two groups to a sustained (1-hour) stressor were observed. Although all testing was conducted in the laboratory, it was believed that this procedure would facilitate generalization of the results to naturalistic settings, at least in the area of duration of the stressor. Finally, to facilitate interpretation of the results, baseline measures were collected during separate counterbalanced relaxation sessions. Ditto has noted that the results of many studies of the relation between family history of hypertension and cardiovascular response to stress are difficult to interpret given group differences in baseline measures. While elevated baseline measures among individuals with a family history of hypertension may represent exaggerated responses to the novelty of the psychophysiological laboratory and anticipation of stress in otherwise healthy people, it is also possible that they indicate the beginnings of disorder. As a result, group differences in responsiveness to stress may be less informative concerning the mechanisms of inheritance of blood pressure. In the present case, eliminating the effects of the anticipation of stress on baseline measures was regarded as important in determining whether differences in regional blood flow at rest and during stress could be observed in people genetically at risk for hypertension before the onset of the disorder.

Subjects and Methods

Twenty healthy young men, 10 with a parental history of hypertension and 10 age-matched individuals without a parental history of hypertension (20–30 years old; mean, 24 years), were recruited from the undergraduate student population of McGill University. All of the offspring of persons with hypertension had just one hypertensive parent. The two groups did not differ significantly in height (mean, 176±5 vs. 179±3 cm, respectively), weight (70.5±5.5 vs. 70.9±7.9 kg), race (all white), or parental age (54±3 vs. 56±5 years).

Although it was not possible to obtain independent measurements of the parents' blood pressures, the presence of hypertension in one parent of the offspring of hypertensive individuals was confirmed by the reported use of antihypertensive medications. In eight of the 10 cases, it was possible to further confirm the status of the hypertensive parents by obtaining from them the name of their current antihypertensive medication (spironolactone [Aldactazide], 2; furosemide [Lasix], 1; captopril [Capoten], 2; prazosin [Minipress], 1; and metoprolol [Lopressor], 2) or by contacting their physician. Although there was considerable variation in frequency of physician contact, all hypertensive and normotensive parents reported visiting their physician at least twice a year.

Each subject participated in two 1-hour experimental sessions at the same time of day, one for the collection of baseline and the other for the collection of stress measurements. Baseline and stress sessions were conducted on two separate days, with the order of the sessions counterbalanced between subjects. Subjects were paid for participating in the study. They were not informed that group differences between individuals with and without a family history of hypertension was the focus of the study. They were told simply that the study concerned patterns of cardiovascular response to an extended laboratory stressor.

Apparatus and Measures

Measurements of systolic, diastolic, and mean arterial blood pressure (in mm Hg) were obtained at 5-minute intervals during the baseline and stress sessions with a Critikon (Tampa, Florida) Dinamap 845XT automatic blood pressure monitor and a thigh cuff on the left leg. Values of blood pressure were corrected for the distance between the cuff and heart level according to the manufacturer's recommendations. Mean values for each of these variables in each 15-minute period during the baseline and stress sessions were calculated. Other physiological measures were obtained with various transducers and electrodes, a Grass (Quincy, Massachusetts) Model 7D polygraph, a set of Med Associates (East Fairfield, Vermont) signal process-
ing modules, and an IBM Personal Computer. Heart rate (beats/min) was derived from an electrocardiogram. Following the method of Williams et al.,21 blood volume pulse (in units) was obtained with a Grass Model PTTL-6 photoplethysmograph attached to the subject’s right second toe. Values of heart rate and blood volume pulse were analyzed on-line by the computer and averaged in 1-minute periods. These values were subsequently averaged in 15-minute periods. Forearm blood flow (ml/min/dl of forearm volume) was measured by using Whitney’s procedure.15,20–22 This procedure relies on mercury-in-Silastic strain gauge plethysmography with intermittent venous occlusion in the left arm by a blood pressure cuff concurrent with isolation of the wrist and hand circulation by a second cuff. Measurements were obtained during minutes 2, 3, and 4 of every 5-minute block during the baseline and stress sessions and averaged by the computer. Forearm vascular resistance was calculated by dividing mean arterial blood pressure by forearm blood flow. Measurements of forearm blood flow and vascular resistance were subsequently averaged in 15-minute periods. Repeated ratings of self-report anxiety were obtained by using a stress “dial” attached to a potentiometer and, in turn, the polygraph and computer. The dial had legends of (0) extremely relaxed, (5) moderately tense, and (10) extremely tense. Subjects were asked to rate their current level of tension throughout the baseline and stress sessions and to indicate this by turning the dial toward or anywhere between these legends. They were asked by the experimenter to provide a rating once every 5 minutes after inflation of the blood pressure cuff.

The stressor was a task used previously in this laboratory: video game play with the avoidance of mild electric shocks that were contingent on performance.23 Video games were played with an Atari video games system. Four challenging but easy-to-learn games were used—Hockey, Maze Craze, Tennis, and Enduro (auto racing). Mild electric shocks were administered by a Farrall Instruments (Omaha, Nebraska) Model AV-2 Behavior Modification Device. Concentric shock electrodes were placed on the ulnar side of the right wrist and elbow.

Procedure
The experiment was conducted in a quiet, carpeted room with a reclining armchair. At the beginning of the subject’s baseline session, the subject was connected to the physiological recording apparatus (housed in a separate room) and asked to sit quietly and relax for 1 hour. The subject’s left arm (from which measures of forearm blood flow were obtained) was supported at a fixed 45-degree angle by a comfortable armrest. At the beginning of the stress session, the subject was introduced to the video games and allowed a brief practice period with each. The subject was then connected to the physiological recording apparatus. The shock electrodes were also attached and the subject was given the video game joystick to operate with his right hand. To minimize extraneous motor activity, the subject’s right arm was lightly tied at the wrist to the arm of the chair. Video game play proceeded for 1 hour. To maintain the subject’s interest, four games were employed, their order determined by a Latin square design. The subject played each game for 15 minutes. Video game play was translated into a shock avoidance procedure by the requirement of certain levels of performance to avoid shocks. Each 15-minute game period was divided into six 2½-minute trials. At the beginning of each trial, the subject was informed of the score necessary to avoid the possibility of receiving a mild electric shock. Criterion scores were determined for each game to reflect performance that was difficult, but not impossible, for subjects with this background (i.e., undergraduate college students) to attain. To deal with practice effects, the criterion score increased for each trial of each game. After each trial, the subject’s score was compared with the criterion. If the criterion was not met, a tone was presented immediately to signal the possibility of receiving a shock from one of the two shock electrodes. However, subjects received no more than three shocks per 15-minute game period, which were limited to a very modest 1.85 mA for 0.3 seconds. This study was approved by the Ethics Committee, Department of Psychology, McGill University. All subjects gave informed, written consent to these procedures.

Data Analyses
To evaluate group differences in baseline values of the variables, 2(parental history hypertension—no parental history hypertension)x4(15-minute period) analyses of variance (ANOVAs) of measurements obtained during the relaxation baseline sessions were conducted. For each subject, four percent change scores for each variable were calculated by subtracting their mean value during the same 15-minute period in the baseline session (e.g., 16–30 minutes) from the value observed during the stress session, dividing by the resting value and multiplying by 100. Two(parental history hypertension—no parental history hypertension)x4(15-minute period) ANOVAs of percent change scores were then conducted. Correlations between percent change scores within 15-minute periods were also calculated. The criterion for statistical significance employed in the study was p<0.05. Means are expressed in their appropriate units±SEM.

Results
Baseline Measures
The ANOVAs of baseline measures revealed no significant differences between individuals with and without a parental history of hypertension in resting blood pressure, heart rate, blood volume pulse, forearm blood flow or resistance, or self-report anxiety. The group effect of the forearm blood flow

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Table 1. Cardiovascular Measurements in First Fifteen Minutes of Baseline Session

<table>
<thead>
<tr>
<th>Variable</th>
<th>Offspring of hypertensives (n=10)</th>
<th>Offspring of normotensives (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>127±3</td>
<td>126±4</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>63±2</td>
<td>65±3</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>70±2</td>
<td>72±4</td>
</tr>
<tr>
<td>Blood volume pulse (units)</td>
<td>2961±209</td>
<td>2984±137</td>
</tr>
<tr>
<td>Forearm blood flow (ml/min/dl)</td>
<td>3.6±0.4</td>
<td>2.6±0.4</td>
</tr>
<tr>
<td>Forearm vascular resistance (MAP/FBF)</td>
<td>28±5</td>
<td>34±6</td>
</tr>
</tbody>
</table>

Values are mean±SEM.

ANOVA approached significance \( F(1,18)=3.50, p=0.08 \), however, indicating a trend toward greater resting blood flow in offspring of hypertensive parents. The mean values of the cardiovascular measurement in the first 15 minutes of the baseline session are displayed in Table 1.

Cardiovascular Responses to Stress

The means of the absolute (raw) changes in cardiovascular activity produced by the stressor are presented in Table 2. These values are provided for reference and are similar to those obtained in other studies in this laboratory.23

The results of the ANOVAs of systolic and diastolic blood pressure percent change scores were identical. None of the effects—group, period, or the interaction of group by period—were significant. Both groups exhibited significant increases in blood pressure in response to the task during all four periods, but there were no significant differences between the groups. The mean systolic blood pressure responses of individuals with and without a parental history of hypertension are displayed in Figure 1. Similarly, both groups exhibited significant decreases in blood volume pulse in response to the task, but did not differ in their response. None of the effects of the blood volume pulse ANOVA were significant. In contrast, the heart rate ANOVA yielded both significant group \( F(1,18)=5.65 \) and period \( F(3,54)=5.80 \) effects. As can be seen in Figure 2, individuals with a parental history of hypertension exhibited significantly greater heart rate responses to the task throughout the session, although the responses of offspring of both hypertensive and normotensive parents declined as the session progressed.

The forearm blood flow ANOVA also yielded a significant group effect \( F(1,18)=8.34 \). As can be

Table 2. Absolute Changes in Cardiovascular Activity Produced by Stressor

<table>
<thead>
<tr>
<th>Variable</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP (mm Hg)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>PH+</td>
<td>19±5</td>
<td>18±6</td>
<td>17±5</td>
<td>18±4</td>
</tr>
<tr>
<td>PH−</td>
<td>12±5</td>
<td>13±4</td>
<td>8±4</td>
<td>11±4</td>
</tr>
<tr>
<td>DBP (mm Hg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PH+</td>
<td>12±3</td>
<td>13±3</td>
<td>14±3</td>
<td>17±3</td>
</tr>
<tr>
<td>PH−</td>
<td>9±2</td>
<td>10±3</td>
<td>9±2</td>
<td>9±2</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PH+</td>
<td>16±5</td>
<td>12±5</td>
<td>10±4</td>
<td>11±5</td>
</tr>
<tr>
<td>PH−</td>
<td>5±3</td>
<td>2±2</td>
<td>0±2</td>
<td>-2±2</td>
</tr>
<tr>
<td>BVP (units)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PH+</td>
<td>-568±320</td>
<td>-581±325</td>
<td>-627±295</td>
<td>-724±303</td>
</tr>
<tr>
<td>PH−</td>
<td>-652±207</td>
<td>-346±147</td>
<td>-435±114</td>
<td>-487±187</td>
</tr>
<tr>
<td>FBF (ml/min/dl)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PH+</td>
<td>5.3±1.4</td>
<td>4.6±1.1</td>
<td>5.0±1.2</td>
<td>4.1±1.1</td>
</tr>
<tr>
<td>PH−</td>
<td>0.7±0.5</td>
<td>0.5±0.5</td>
<td>0.4±0.4</td>
<td>0.2±0.4</td>
</tr>
<tr>
<td>FVR (MAP/FBF)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PH+</td>
<td>-14±5</td>
<td>-12±6</td>
<td>-13±5</td>
<td>-11±6</td>
</tr>
<tr>
<td>PH−</td>
<td>-5±5</td>
<td>-5±5</td>
<td>-5±6</td>
<td>-3±5</td>
</tr>
</tbody>
</table>

Values are mean±SEM.

SBP, systolic blood pressure; PH+, parental history of hypertension; PH−, no parental history of hypertension; DBP, diastolic blood pressure; HR, heart rate; BVP, blood volume pulse; FBF, forearm blood flow; FVR, forearm vascular resistance; MAP, mean arterial pressure.
FIGURE 1. Line graph showing mean systolic blood pressure responses (in percent change±SEM) of offspring of hypertensive (●) and normotensive (○) parents to video game play. Although both groups exhibited significant elevations of blood pressure throughout the stress session, none of the effects of the analysis of variance (ANOVA) were significant.

seen in Figure 3, individuals with a parental history of hypertension exhibited significantly greater forearm blood flow responses to the task than individuals without a parental history of hypertension throughout the session. Similarly, the group effect in the forearm vascular resistance ANOVA approached significance [F(1,18)=3.41, p=0.08], related to the fact that offspring of hypertensive parents exhibited somewhat greater decreases in forearm vascular resistance than offspring of normotensives (-37±12 vs. -1±15%).

Behavioral Measures

There were no significant differences between offspring of hypertensive and normotensive parents in task performance. Overall, offspring of hypertensive individuals met the criterion and avoided the possibility of receiving a shock 45% of the time, compared with 48% of the time for offspring of normotensive individuals. However, the ANOVA of self-report anxiety ratings revealed a significant group effect [F(1,18)=5.40]. As can be seen in Figure 4, offspring of hypertensive individuals generally reported greater increases in anxiety during the stress session. The interaction of group by period approached significance [F(3,54)=2.64, p=0.06], which suggested a habituation of the effect by the end of the session. In fact, the difference in the responses of offspring of hypertensive and normotensive parents to the final 15 minutes of video game play was not significant [t(18)=0.86, NS].

Correlations Between Measures

Correlations between responses to each of the four 15-minute periods of video game play in each dependent measure were calculated. The only reliable correlations (i.e., significant in each of the four 15-minute periods) were between heart rate and forearm blood flow responses. The correlation between heart rate response to the first 15 minutes of video game play and forearm blood flow response to the first 15 minutes of play was r=0.49. The
correlations between heart rate and forearm blood flow responses to the second, third, and fourth 15-minute periods of video game play were 0.40, 0.44, and 0.67, respectively.

Discussion

The results of the present study indicate the importance of including measures other than blood pressure when studying the responsiveness of individuals at risk for hypertension. Although the offspring of hypertensive parents in the present study were normotensive and exhibited "normal" blood pressure responses to stress, they exhibited a hemodynamic pattern of response to the task that was quite different from the pattern displayed by offspring of normotensive parents. The absence of group differences in blood pressure response may have been due to increased vasodilation in the skeletal muscles of the offspring of hypertensive parents that offset the apparent difference in cardiac responsiveness. This response pattern, which is similar to the pattern elicited by physical exercise, may be another reason for the inconsistent findings of higher blood pressure responsiveness to psychological stress among individuals with a family history of hypertension.  

The observations that 1) offspring of hypertensive individuals exhibited enhanced forearm vasodilation and heart rate responses to the task, 2) there were no group differences in other cardiovascular measurements, and 3) forearm blood flow and heart rate responses to the task were significantly correlated suggest that the groups differed in sympathetic nervous system, and possibly β-adrenergic, response to the task. Cardiac responses to active coping tasks such as the one used in the present study seem to be quite susceptible to β-adrenergic blockade with propranolol. Further, β-adrenergic activity in the skeletal muscles promotes vasodilation.

The present results allow no conclusions concerning the mechanisms of enhanced sympathetic nervous system activity, but possibilities include greater receptor sensitivity, enhanced adrenal medullary activity, and greater sympathetic nervous system outflow. Not surprisingly, given the diverse genetic influences on cardiovascular reactivity in the spontaneously hypertensive rat, evidence for each of these hypotheses can be found. For example, for the hypothesis that individuals with a family history of hypertension display greater peripheral adrenergic receptor sensitivity, several researchers have found that offspring of hypertensive parents exhibit exaggerated pressor responses to infused norepinephrine. In regard to the second hypothesis, Falkner et al found that offspring of hypertensive parents exhibited greater plasma catecholamine responses to stress than offspring of normotensive parents. Williams et al found that the differences in forearm blood flow responsiveness to stress between Type A and Type B individuals were related to differences in plasma epinephrine and norepinephrine levels.

Finally, it seems likely central nervous system effects and enhanced sympathetic nervous system outflow may be involved as well. In this regard, the group differences in self-report anxiety in the present study are intriguing. Jorgensen and Houston found that offspring of hypertensive parents reported greater increases in subjective anxiety after participating in a shock avoidance task than offspring of normotensive parents. However, Manuck et al found no group differences in affective response to a mental arithmetic task that elicited significant differences in heart rate and diastolic blood pressure responses. It is possible that differences in affective reactivity between individuals with and without a family history of hypertension are elicited only by fairly intense stressors (e.g., shock avoidance). It is tempting to point to evidence of high emotionality in spontaneously hypertensive rats and suggest that genetic factors might contribute to a general hyperresponsiveness to environmental stimulation mediated by the limbic and hypothalamic areas that can be observed in physiological, behavioral, and affective parameters. In a series of studies, Baer and coworkers found that families with hypertensive fathers tend to exhibit more negative nonverbal behaviors (e.g., gaze aversion) than families without hypertensive parents, and that there may be some relation between the frequency of negative nonverbal behaviors in parents and the blood pressure levels of children.

On the other hand, there are a number of other, possibly more parsimonious, explanations for enhanced affective responsiveness to stress among individuals with a family history of hypertension. For example, Katkin in a review reported that he and others found that 1) perception of cardiac activity is related to affective experience, 2) the more intense the stressor, the greater the perception of cardiac activity, and 3) men tend to be more aware of cardiac activity than women. As a result, the affective responses of the offspring of hypertensive parents may have been related to the perception of their enhanced cardiovascular responsivity. This hypothesis is particularly plausible in the present case given the use of men as subjects and a fairly intense stressor that produced detectable increases in heart rate among offspring of hypertensive parents. Interestingly, group differences in self-report anxiety disappeared at the end of the stress session when the heart rate responses of both groups had declined.

In summary, the results of the present study suggest that healthy young offspring of hypertensive and normotensive parents exhibit different patterns of hemodynamic response to stress in the absence of differences in resting blood pressure or blood pressure responsiveness to stress. Further, the pattern of response displayed by offspring of hypertensive individuals may be accompanied by increased psychological distress and may persist for at least an hour under conditions of continuing
stress. Future research should examine the mechanisms of altered regional blood flow in offspring of hypertensive parents and the role of these mechanisms in the natural history of hypertension.

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