Glomerular Hyperfiltration During Sympathetic Nervous System Activation in Early Essential Hypertension

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Abstract. Glomerular hyperfiltration may be important for the development of essential hypertension. Both the renin-angiotensin system and the sympathetic nervous system influence renal hemodynamic regulation. To test the hypothesis that glomerular hyperfiltration can be unmasked by sympathetic nervous system activation, renal hemodynamics and humoral components of the renin-angiotensin system were examined at rest and during mental stress in 45 young normotensive healthy subjects and 37 young people with mild essential hypertension. GFR and renal plasma flow (RPF) were determined with inulin and para-aminohippuric acid clearance at rest and during stress. At rest, RPF, GFR, filtration fraction, plasma renin activity, angiotensin (Ang) II concentrations, and serum aldosterone values were similar in normotensive and hypertensive subjects. After stress, blood pressure increased ($P < 0.01$), but this was nearly identical in normotensive and hypertensive subjects (7.05 ± 6.9 *versus* 7.03 ± 4.6 mmHg, NS). The decrease in RPF (−27 ± 54 *versus* −22 ± 25 ml/min per 1.73 m^2, NS) was also similar in the two groups. In contrast, the increase in GFR (+10.5 ± 7.2 *versus* 6.08 ± 5.7 ml/min per 1.73 m^2, $P < 0.001$) and filtration fraction (+2.48 ± 1.38 *versus* 1.82 ± 1.49%, $P < 0.05$) was more marked in hypertensive than in normotensive subjects. The concomitant increase in Ang II concentrations was greater in hypertensive than in normotensive subjects (+4.6 ± 1.0 *versus* −1.0 ± 0.45 pg/ml, $P < 0.001$). The increase in GFR during mental stress was correlated with the increment in Ang II concentrations ($r = 0.39$, $P < 0.001$). Compared with the placebo control phase, blockade of the renin-angiotensin system with an angiotensin-converting enzyme inhibitor attenuated the increase in GFR during stress in hypertensive (8.04 ± 5.01 *versus* 10.1 ± 5.7 ml/min per 1.73 m^2, $P < 0.05$), but not in normotensive, subjects. Even in early essential hypertension, glomerular hyperfiltration is evident during sympathetic nervous system activation, which is mediated by postglomerular vasoconstriction. This early stress-induced glomerular hyperfiltration may contribute to, or trigger, the development of essential hypertension. (J Am Soc Nephrol 8: 893–900, 1997)

Several lines of evidence suggest that the sympathetic nervous system contributes to the pathogenesis of essential hypertension by affecting the renal circulation. Renal denervation delayed the development of hypertension in young, spontaneously hypertensive rats (1,2). Conversely, chronic renal nerve stimulation evoked hypertension in dogs (3). In animal models, exposure to mental stress increased renal sympathetic nerve activity, reduced renal blood flow by vasoconstriction predominantly of the efferent arteriole, and modulated tubular sodium reabsorption (4). In hypertensive men, exaggerated renal vasoconstriction and stimulation of the renin-angiotensin system were observed immediately after exposure to mild mental stress (5). Angiotensin (Ang) II interacts with the sympathetic nervous system in different ways, including regulation of central mechanisms, facilitation of noradrenergic transmission in several organs, and augmentation of sympathetic nervous system stimulation in resistance vessels and the heart (6–10). Thus, an interaction among Ang II, the sympathetic nervous system, and the kidney could play an important role in the control of renal circulation and volume homeostasis. Previously, we observed that Ang II modulates the renal effects of centrally mediated changes in the sympathetic nervous system (11).

Thus far, the impact of centrally mediated sympathetic nervous system activation on the renal circulation in humans has been examined only with respect to renal plasma flow (RPF); however, the effects on GFR and filtration fraction (FF) have not been systematically examined (5). In a pilot study, we observed that mental stress caused an acute increase in GFR and FF in normotensive healthy subjects (12), a finding that is in agreement with the observed vasoconstriction at the postglomerular site after stimulation of renal sympathetic nerve activity (13–15). In patients with essential hypertension, glomerular hyperfiltration was found to be related to left ventricular hypertrophy and to baseline renal function, even in the presence of antihypertensive treatment (16,17). Low birth weight associated with glomerular hyperfiltration at the single nephron level was reported to predict the subsequent age-related increase in blood pressure (18–19). Similarly, in

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healthy kidney donors who display a relative glomerular hyperfiltration in their remaining nephrons, the incidence of hypertension was found to be increased in all but two studies (20). In a most recent study, a 50% reduction of renal mass had no effect on the prevalence of hypertension; subjects with greater than 50% reduction, however, did have a small increase in blood pressure (21). These studies support the notion that glomerular hyperfiltration may increase the risk of developing essential hypertension in humans (18–21).

In this study, we examined the effects of mental stress on renal hemodynamics. We found that we could provoke a relative hyperfiltration in young subjects with mild hypertension. We then tested whether the hemodynamic changes observed during stress were mediated by the renin-angiotensin system.

Materials and Methods

Study Population

Forty-five young normotensive healthy control subjects without a family history of hypertension and 37 young white male subjects with mild essential hypertension (World Health Organization stage I-II) were enrolled in the study. Normotension was confirmed when the systolic blood pressure and the diastolic blood pressure were <140 mmHg and <90 mmHg, respectively, on all of four screening blood pressure readings. If the average systolic blood pressure was ≥140 mmHg (n = 26) or the diastolic blood pressure exceeded was ≥90 mmHg during screening (n = 19), the subjects were classified as having mild essential hypertension. All screening blood pressure readings were taken in the sitting position after 5 min of rest with a standard mercury sphygmomanometer on two different occasions at least 2 wk apart (according to World Health Organization recommendations). The cuff size was adjusted according to arm circumference. Hypertensive subjects were identified by screening students for high blood pressure at the university campus in Nuremberg and Erlangen, Germany. None of the subjects had ever received cardiovascular medication, none followed any specific diet, and none had secondary forms of hypertension or target organ damage. Exercise stress testing or detailed evaluation of renal arteries (intra-arterial digital subtraction angiography) and analysis of hormones and endocrine metabolites were done when clinically indicated. Normotensive subjects participated as volunteers and underwent the same complete routine clinical workup to ensure a normal cardiovascular system. All subjects underwent echocardiography to allow the determination of cardiac dimensions as described for our laboratory earlier (16,17). Furthermore, after recruitment and classification, all subjects underwent 24-h ambulatory blood pressure measurements (Space Labs, Kaarst, Germany). A questionnaire given to all participants (n = 82) asked about birth weight and body length at birth, according to hospital records or the mother's recollection. Reliable birth weight and length data were obtained in 44 subjects. Informed written consent was obtained from each individual, and the study protocol was approved by the university's committee on the protection of human subjects.

Study Design and Experimental Methods

Participants were asked to refrain from smoking and drinking coffee or alcoholic beverages on the day before the studies. The 45 normotensive control subjects and the 37 subjects with mild essential hypertension were randomly allocated either to receive placebo for 1 wk (baseline examination) followed by a washout period of 7 d, and then angiotensin-converting enzyme (ACE) inhibition with 2.5 mg of cilazapril once daily by mouth for another week (ACE inhibitor phase), or the sequence of placebo and cilazapril was reversed. The study protocol followed a randomized double-blind crossover design. Pill counts were performed to ensure compliance, and patients were informed that serum drug levels would be measured. Evaluation of renal hemodynamics and the humoral status of the renin-angiotensin system was performed at the end of the 1-wk placebo and cilazapril phase, respectively.

To determine RPF and GFR, we applied the constant infusion technique without urine sampling as suggested by Cole *et al.* and other investigators (22–25). Briefly, under steady-state conditions the excreted amount of para-aminohippuric acid (PAH) (Nephrotest®, MSD, Great Britain) and inulin (Inutest®, Linz, Austria) is equal to the infused dose of the compounds. Because PAH is not completely excreted in normal subjects, the method overestimates the true PAH clearance by approximately 10 to 20% (26, 27). However, the bias is constant because the extraction of PAH by the kidney is constant (approximately 90%) and similar in subjects if the RPF is >300 ml/min (22, 25). The technique allows the avoidance of bladder catheterization or reliance on spontaneous voiding. The major advantage for our purpose was the fact that the hemodynamic response during mental stress test was not influenced by any manipulations of bladder catheters or by spontaneous voiding, both of which affect the cardiovascular hemodynamic parameters we wished to observe. In previous studies, we have found the method to be valid and reliable, especially in the face of provocative maneuvers (12).

One intravenous line was inserted for infusion and another for withdrawing blood samples in the opposite arm. After a bolus injection, a constant infusion was given for a total of 150 min to achieve steady-state conditions. Mental stress test was applied for 30 min and blood samples were collected at the end of the stress period (minute 145 and minute 150). The doses for bolus injection and constant infusion of inulin and PAH were adjusted to body weight (12). All patients had normal serum creatinine and creatinine clearance values. PAH was measured by the method of Bratton and Marshall as modified by Smith *et al.* (26). Inulin was measured indirectly by converting inulin to fructose and subsequently measuring fructose by enzymatic method (716260; Boehringer Mannheim, Mannheim, Germany) as outlined in detail elsewhere (24). Each blood sample taken at rest and during stress was measured in duplicate, and coefficients of variation were <5% for each determination. The FF was calculated by dividing the GFR by the RPF.

To activate the sympathetic nervous system with mental stress, we used a modified time reaction task device (Wiener Determinationsgerät, Vienna, Austria) with a computerized feedback system to hold stimulus intensity constant over 30 min of stress test (28). The speed of the task was adjusted to the performance of each participant so that the stress intensity was constant over a longer period of time. Compared with other stress tests, the time reaction task evokes a rather mild hemodynamic response and allows the stressing of subjects up to 30 min without loss of cardiovascular response during stress (12, 28). The constant infusion technique without urine collection required a steady state of at least 30 min to achieve a new steady-state condition after stress exposure (12). Blood pressure was measured every minute by means of an oscillometric device (Dinamap, Norderstedt, Germany).

Blood samples for measuring the endocrine parameters of the renin-angiotensin system were withdrawn at the end of the resting period after the subjects had been recumbent for 2 h (on an *ad libitum* sodium diet) and at the end of mental stress tests. Blood was withdrawn in prechilled tubes, immediately centrifuged at 0°C, and stored at −18°C. Plasma renin activity, plasma Ang II, and serum aldosterone concentrations were all determined by RIA (29–31). In addition,

in the last 40 subjects included plasma catecholamines were measured by HPLC and electrochemical detection after separation of the catecholamines with a reversed phase (Waters Novopark, C-18 column), as described in detail (32).

All data were analyzed using the PC version of the Statistical Package for the Social Sciences (33). Unpaired *t* tests were used comparing normotensive and hypertensive subjects. Paired *t* tests were done for the comparisons between rest and stress values. Pearson correlation coefficients were calculated when indicated. Results are given as mean ± SD in the tables and mean ± SEM in the figures when normotensive and hypertensive subjects were directly compared, respectively. Renal hemodynamic values were corrected for body surface area because normotensive and hypertensive subjects differed in body size and surface area.

Results

The baseline demographic and clinical characteristics of the subjects are given in Table 1. The hypertensive subjects had a greater body mass index (although well within the normal range) and a greater body surface area than the normotensive subjects. They had higher blood pressures and also a greater left ventricular mass index and a greater relative wall thickness than the normotensive subjects. GFR, RPF, plasma renin activity, Ang II levels, and aldosterone concentrations were not different between hypertensive and normotensive subjects.

Table 2 shows the effects of mental stress on blood pressure, renal, and humoral parameters. Stress caused a similar increase in systolic, diastolic, and mean arterial blood pressure in hypertensive and normotensive subjects. GFR increased by 10 ml/min in hypertensive subjects compared with 6 ml/min in normal subjects, even though the 22 to 27 ml/min decrease in RPF in the two groups was not significantly different. Even after taking body mass index into account, we still observed a more marked increase in GFR ($P < 0.004$) and FF ($P < 0.05$) in hypertensive than normotensive individuals. The renal responses resulted in a borderline difference in FF in response to stress in the two groups. Plasma epinephrine increased significantly in normotensive and hypertensive subjects without any difference between the two groups, whereas plasma norepinephrine did not change significantly. Plasma renin activity decreased in normal and increased in hypertensive subjects ($P = 0.05$), which also was the case for Ang II ($P < 0.001$). The effect on aldosterone values, however, was not different for normotensive and hypertensive subjects. The lower portion of Table 2 shows the same responses under the influence of ACE inhibition. After 1 wk of treatment with cilazapril, mean blood pressure at rest remained unchanged in normotensive subjects (82 ± 7 *versus* 81 ± 7 mmHg), but dropped in hypertensive subjects (94 ± 10 *versus* 89 ± 9 mmHg, $P < 0.01$). We observed no change in the blood pressure response to mental stress (mean blood pressure increase: 6.5 ± 5 *versus* 8.0 ± 4.5 mmHg in normotensive subjects and 6.3 ± 4 *versus* 6.6 ± 4 mmHg in hypertensive subjects). In contrast, renal hemodynamic responses and changes in Ang II concentrations differed after ACE inhibition compared with baseline values. The increase in GFR was attenuated in hypertensive subjects after ACE inhibition (10 ± 8 *versus* 8 ± 6 ml/min, $P < 0.02$) but was not affected in normotensive subjects. Thus, with ACE inhibition, the increase in GFR in response to stress was no longer different between normotensive and hypertensive sub-

Table 1. Clinical characteristics of the examined subjects[a]

Characteristic	Normotensive $n = 45$	Hypertensive $n = 37$	*P* Value *n versus* H
Age	26 ± 3	26 ± 2	NS
Height (m)	1.82 ± 0.07	1.82 ± 0.8	NS
BMI (kg/m^2)	22.7 ± 2.03	24.6 ± 2.86	$P < 0.001$
BSA (m^2)	1.96 ± 0.13	2.03 ± 0.14	$P < 0.01$
Screening BP			
systolic (mmHg)	123 ± 8	145 ± 10	$P < 0.001$
diastolic (mmHg)	74 ± 7	90 ± 6	$P < 0.001$
Mean BP at rest (mmHg)	82 ± 7	94 ± 10	$P < 0.001$
LV mass (g/m^2)	109 ± 16	124 ± 21	$P < 0.001$
Relative wall thickness (−)	0.35 ± 0.04	0.38 ± 0.05	$P < 0.001$
GFR (ml/min per 1.73 m^2)	112 ± 13	114 ± 12	NS
RPF (ml/min per 1.73 m^2)	603 ± 118	599 ± 96	NS
FF (%)	19.3 ± 4	19.3 ± 2.8	NS
Plasma renin activity (ng AI/ml per h)	1.9 ± 0.9	1.8 ± 1.2	NS
Ang II (pg/ml)	11.7 ± 1.8	10.2 ± 0.9	NS
Aldosterone (pg/ml)	136 ± 14	169 ± 22	NS
Norepinephrine (pg/ml)[b]	296 ± 102	320 ± 86	NS
Epinephrine (pg/ml)[b]	32 ± 16	38 ± 9	NS

[a] BMI, body mass index; BSA, body surface area; LV, left ventricular; GFR, glomerular filtration rate; RPF, renal plasma flow; FF, filtration fraction; Ang, angiotensin.

[b] Data were obtained in only 20 subjects of each group.

Table 2. Glomerular hyperfiltration during sympathetic activation at the onset of essential hypertension[a]

Parameter	Normotensives $n = 45$	Hypertensive $n = 37$	P Value n *versus* H
Change during stress			
SBP (mmHg)	10 ± 7	11 ± 7	NS
DBP (mmHg)	3 ± 13[b]	4 ± 4[b]	NS
MAP (mmHg)	7 ± 7[b]	7 ± 5[b]	NS
GFR (ml/min per 1.73 m^2)	6 ± 7[b]	10 ± 6[b]	$P < 0.001$
RPF (ml/min per 1.73 m^2)	−27 ± 54[c]	−22 ± 25[b]	NS
FF (ml/min per 1.73 m^2)	1.8 ± 1.7[b]	2.5 ± 1.4[b]	$P = 0.069$
plasma renin activity (ngAl/ml per h)	−0.23 ± 0.6[c]	0.11 ± 0.9	$P = 0.053$
Ang II (pg/ml)	−1.0 ± 3.0	4.6 ± 5.3[d]	$P < 0.001$
aldosterone (pg/ml)	−27 ± 53[b]	−17 ± 34[c]	NS
norepinephrine (pg/ml)	−10 ± 65	3 ± 72	NS
epinephrine (pg/ml)	13 ± 14[b]	11 ± 15[c]	NS
Change during stress after ACE inhibition			
SBP (mmHg)	9 ± 6[b]	11 ± 9[b]	NS
DBP (mmHg)	4 ± 3[b]	5 ± 5[b]	NS
MAP (mmHg)	6 ± 5[b]	8 ± 6[b]	NS
GFR (ml/min per 1.73 m^2)	5.0 ± 5.0[b]	8 ± 5[b]	0.043
RPF (ml/min per 1.73 m^2)	−31 ± 63[d]	−37 ± 41[c]	NS
FF (ml/min per 1.73 m^2)	1.7 ± 1.99[b]	2.4 ± 1.3	NS
plasma renin activity (ngAl/ml)	−4.0 ± 5.4[c]	−1.8 ± 4.4[d]	NS
Ang II (pg/ml)	−0.64 ± 1.4[d]	1.07 ± 5.5[d]	NS
aldosterone (pg/ml)	−18 ± 28[c]	−18 ± 42[c]	NS
norepinephrine (pg/ml)[e]	−33 ± 71	−62 ± 97	NS
epinephrine (pg/ml)[e]	6 ± 11[b]	9 ± 22[d]	NS

[a] SBP, systolic BP; DBP, diastolic BP; MAP, mean arterial pressure. Other abbreviations as in Table 1.
[b] $P < 0.001$, stress *versus* baseline.
[c] $P < 0.01$, stress *versus* baseline.
[d] $P < 0.05$, stress *versus* baseline.
[e] Data were obtained in only 20 subjects of each group.

jects. Moreover, the increase in Ang II in response to stress that was observed with placebo treatment in hypertensive subjects was no longer evident.

We observed a highly significant direct correlation between the change in Ang II levels and the change in GFR in response to stress in the whole study population during the placebo phase, as shown in Figure 1. The greater the stress-induced increase in Ang II, the greater the stress-induced increase in GFR ($r = 0.39$; $P < 0.001$). A similar relationship was observed in hypertensive individuals ($r = 0.42$; $P < 0.05$), but not in normotensive subjects. We identified similar significant correlations between the stress-induced change in GFR and relative cardiac wall thickness ($r = 0.33$; $P < 0.01$) and left ventricular mass index ($r = 0.23$; $P < 0.05$), as shown in Figure 2. If analyzed separately, the corresponding correlations for relative wall thickness were of borderline significance for the hypertensive group (hypertensive: $r = 0.31$; $P = 0.11$; normotensive: $r = 0.26$; $P = 0.09$). The GFR and Ang II responses to mental stress, with and without ACE inhibition, are displayed graphically in Figure 3. ACE inhibition attenuated the increase in GFR during mental stress and blocked the increase in plasma Ang II concentrations in hypertensive subjects, but had no effect on the responses in normotensive subjects.

Despite having only 44 values, we found that birth weight was inversely correlated with 24-h ambulatory blood pressure in our subjects. The lower the birth weight, the greater the systolic ambulatory 24-h blood pressure ($r = -0.47$; $P < 0.01$). For diastolic blood pressure, a similar correlation was found ($r = -0.47$; $P < 0.02$). Because birth weight was correlated with obesity, partial correlation coefficients were calculated and systolic blood pressure remained inversely correlated with birth weight (partial $r = -0.47$; $P < 0.02$). Birth weight was not related to GFR, RPF, or FF at rest or during mental stress, even after the potential influence of obesity, baseline GFR, and blood pressure was taken into account. Thus, glomerular hyperfiltration during sympathetic activation appeared not to be related to low birth weight in this small sample.

Discussion

The most striking result of our study is that sympathetic activation during mental stress provoked glomerular hyperfiltration and concomitantly increased Ang II in young, mildly

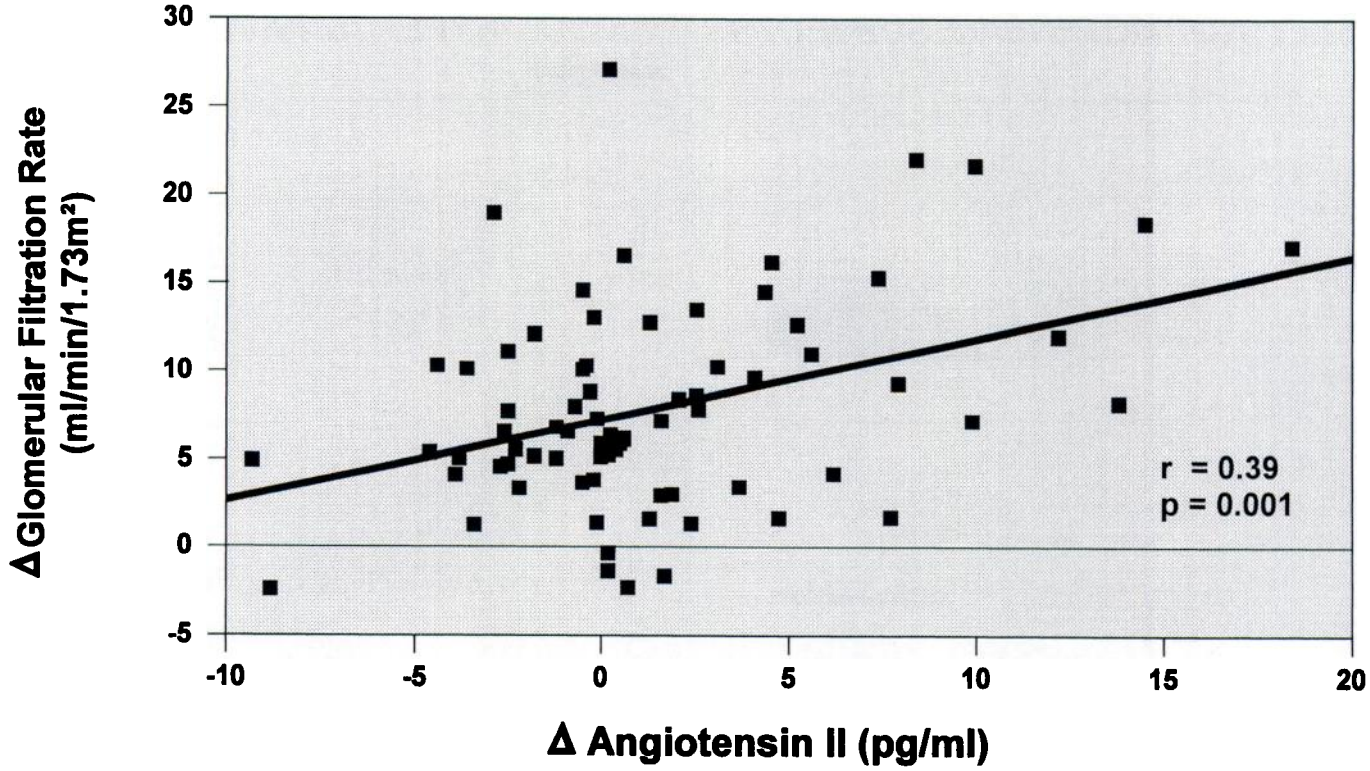

Figure 1. Relationship between the mental stress-induced change in Angiotensin (Ang) II concentrations and the change in GFR in the entire population.

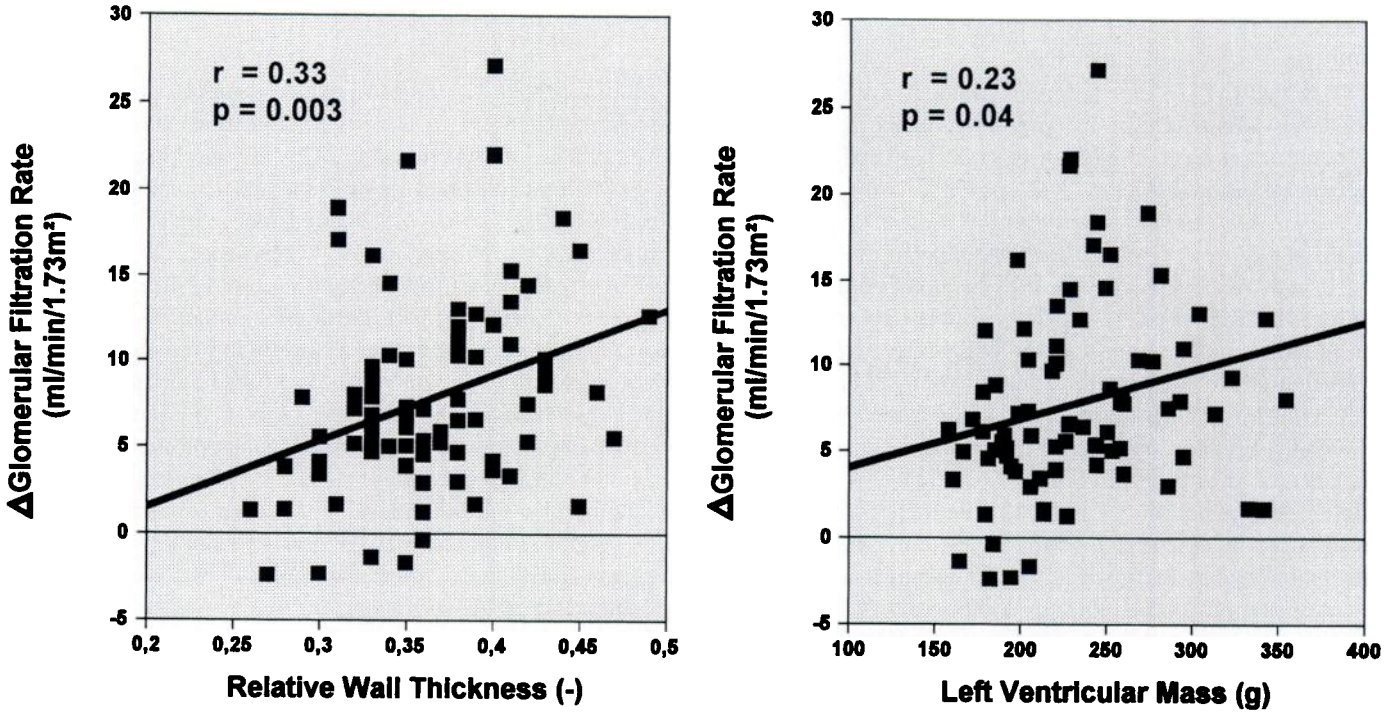

Figure 2. (Left) Relationship between the relative cardiac wall thickness and mental stress-induced change in GFR in the entire population. (Right) Similar relationship between left ventricular mass and the change in GFR.

hypertensive subjects compared with normotensive control subjects. The increase in GFR during mental stress was further related to early cardiac structural adaptation, a finding that suggests that Ang II may be a common denominator in this relationship. Ang II exerts a growth stimulating action on the myocardium in experimental animals, and most likely in hu-

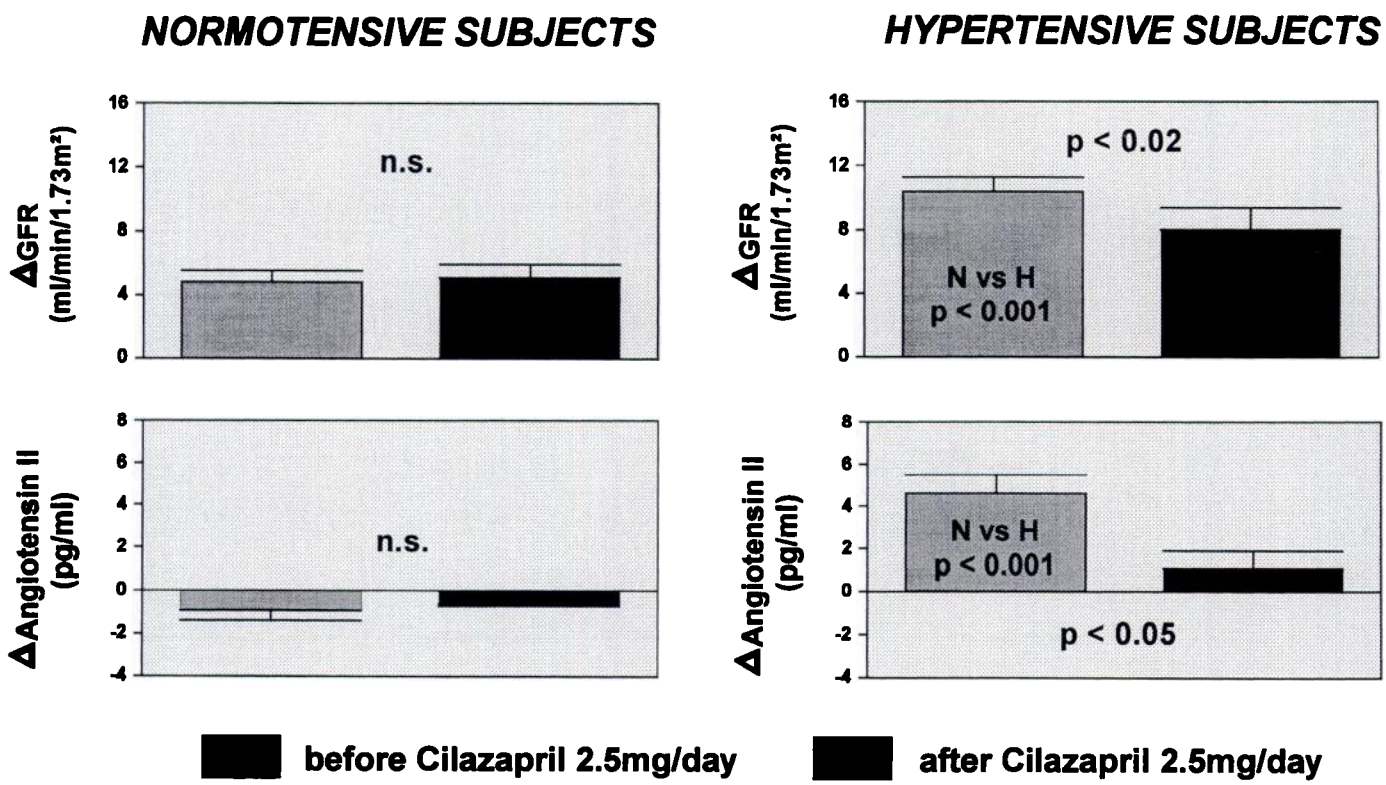

Figure 3. (Left) Mental stress-induced change in GFR and change in Ang II with placebo or with cilazapril in normotensive subjects. No significant effects of cilazapril were observed. (Right) Mental stress-induced change in GFR and change in Ang II with placebo or with cilazapril in hypertensive subjects. Cilazapril decreased the change in GFR and blocked the increase in Ang II observed with placebo.

mans as well (34–38). Furthermore, endogenous and low-dose exogenous administration of Ang II produced an increase in GFR and a decrease in RPF in isolated perfused kidneys by preferential vasoconstriction at the postglomerular site (39). In our human subjects, we found that the change in GFR due to mental stress was correlated with the change in Ang II, consistent with vasoconstriction at the postglomerular site. These findings are supported by previous animal experiments from our group, demonstrating a modulating effect of the central sympathetic activation on the kidneys by Ang II (11). Interestingly, changes in angiotensin II and aldosterone in response to a mental arithmetic task of low stimulus intensity were not parallel and were even discordant.

In the second part of our study, the renin-angiotensin system was blocked by cilazapril, and the increase in GFR was attenuated in the hypertensive subjects, whereas the increase in Ang II concentrations was blocked completely. No significant change was observed in normotensive subjects after ACE inhibition. An increased sensitivity of the renal vasculature to the infusion of Ang II, as well as a renal vasoconstrictor response to intravenous saline infusion, has been described in the offspring of hypertensive patients (40,41). These findings support our hypothesis that the observed glomerular hyperfiltration (evident in the early stage of essential hypertension during sympathetic activation) is mediated by Ang II, because the hyperfiltration was corrected by ACE inhibition.

Derangements in renal function may promote the development of essential hypertension (41, 42). An increase in preglomerular resistance is a likely hemodynamic alteration in the development of hypertension (41). In the Dutch offspring study, a slight reduction in RPF was noted in subjects with a positive family history of hypertension (25). RPF decreased further with the progression of hypertension (17, 25). However, the maintenance of GFR within normal limits, despite a progressive decline in RPF (with concomitant increased FF), also suggests increased efferent arteriolar resistance (39). It was suggested by Guyton *et al.* that glomerular capillary pressure is not increased in essential hypertension because of an increase in preglomerular resistance, which prohibits the transmission of an increased pressure in the systemic circulation to the glomerular bed (43). However, their calculations are based on several assumptions that are derived from data under resting, not under stress, conditions. Previously, we found that endogenous Ang II modulated the renal impact of centrally mediated changes in sympathetic nerve activity in conscious rats (11). Furthermore, during stress, renal sympathetic nerve activity was significantly higher in spontaneously hypertensive rats than in Wistar Kyoto rats and remained elevated throughout the stress period (44). Hence, the hemodynamic intraglomerular situations differ, whether examined at rest or during stress. Moreover, direct measurements of the intraglomerular pressure showed a higher baseline glomerular pressure and a greater increase with phenylephrine infusion in spontaneously hypertensive rats than in normotensive Wistar Kyoto rats (45).

Thus, we hypothesize that early in the development of essential hypertension, the interaction of Ang II with central sympathetic outflow to the kidneys may lead to postglomerular vasoconstriction and glomerular hyperfiltration during a stressful episode.

The reactivity of the circulation to various vasoconstrictor agents in normotensive and hypertensive subjects was described in an earlier report (46). The infusion of epinephrine in normotensive subjects produced an increase in GFR and FF, whereas norepinephrine did not change GFR, but instead reduced RPF. Low-intensity mental stress, as used in this study, is characterized by an increase in epinephrine concentrations without significant changes in norepinephrine levels (46). A stress-induced increase in GFR and FF has been repeatedly reported in normotensive subjects (12,47,48). However, an interaction between Ang II and the sympathetic nervous system activation was not considered in earlier studies (11,44). Nevertheless, previous experiments using a mild psychological stimulus, similar to the model we used, disclosed an increase in Ang II concentrations in hypertensive subjects and a decrease in normotensive subjects (5). These observations are in accord with our findings. Unfortunately, a complete hemodynamic profile was not assessed in these studies because GFR was not measured. In another report that included hypertensive patients, a decrease in GFR was observed (47,49). However, these data cannot be compared to our findings, because a very strong stressful stimulus was used in those studies, older hypertensive patients were examined, and the patients had been treated previously (49). The intensity and type of stress are known to influence the hemodynamic and endocrine profile observed after sympathetic activation (46,50).

We also attempted to examine the effects of low birth weight in our study and its relation to renal hemodynamics. Low birth weight is associated with reduced nephron number, thereby eliciting compensatory glomerular hyperfiltration in the remaining nephrons (51,52). Our hypothesis was that low birth weight is linked to high blood pressure in later life due to changes in renal hemodynamics, namely glomerular hyperfiltration, during sympathetic activation. The fact that birth weight was not directly related to renal hemodynamics at rest or to glomerular hyperfiltration during sympathetic activation argues against the notion that glomerular hyperfiltration is the primary pathogenic link between low birth weight and high blood pressure in later life. Our birth weight data must necessarily be considered preliminary because of the small number of subjects able to supply such information.

In conclusion, we found glomerular hyperfiltration after stress-induced sympathetic activation in subjects with early mild essential hypertension. Because the phenomenon was attenuated with ACE inhibition, our data suggest that this renal hemodynamic abnormality is mediated by postglomerular vasoconstriction. Because hyperfiltration may lead to chronic renal injury by various mechanisms (51,52), our findings may provide a link between the proposed hypertensinogenic effects of stress and hypertension-induced renal injury.

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