Reduced Reflex Sympathoinhibition in Adolescents with Hypertensive Parents

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It has often been suggested that impaired baroreflex is a permissive mechanism that allows blood pressure to remain elevated not only in experimental1–5 but also in clinical6–8 hypertension. Impaired baroreflex may also be involved in the development of hypertension as we have recently found that it preceded the elevation of blood pressure in Dahl salt-sensitive rats1,5,9 and centrally salt loaded Sprague-Dawley rats. However, it is difficult to estimate the baroreflex regulation in a subject with essential hypertension when his blood pressure level is still normotensive. The present studies aimed to determine whether the baroreflex regulation of normotensive or borderline hypertensive subjects with hypertensive parents differed from that of normotensive subjects with no family history of hypertension.

The participants in the study, 33 male adolescents aged 18 to 23 years old, were divided into the following 3 groups. The first group, termed NT (FH–), consisted of 12 normotensive subjects who had no family history of hypertension for at least 3 generations. The second group, NT (FH+), consisted of 10 normotensive subjects each of whom had at least one parent with essential hypertension. The third group, BHT (FH+), consisted of 11 borderline hypertensive subjects whose systolic pressures in the sitting position were higher than 140 mmHg on 3 different occasions and each of whom had at least one parent with essential hypertension. Baseline arterial pressures and heart rate in BHT (FH+) group were significantly higher ($p < 0.05$) than those in either NT (FH–) or NT (FH+) (i.e., SBP: 128 ± 2 (Mean ± SEM) mmHg, DBP: 78 ± 2 mmHg, MBP: 95 ± 2 mmHg, HR: 68 ± 2 beats/min in NT (FH–); 128 ± 2, 80 ± 2, 96 ± 2, 66 ± 2 in NT (FH+); 148 ± 3, 89 ± 3, 108 ± 2, 78 ± 2 in BHT (FH+), respectively), but none of the differences between normotensive subjects was significant. Averaged mean ages were 21.4 ± 0.5 years in NT (FH–), 21.7 ± 0.3 in NT (FH+), and 22.0 ± 0.3 in BHT (FH+). They did not differ between groups.

Cardiovascular and Sympathetic Measurement

Pulsatile arterial pressure was continuously recorded by the non-invasive device which was developed in our laboratory. Heart intervals were measured from an ECG recorded by chest electrodes.

A tibial nerve was used to identify muscle sympathetic nerve activity in a subject lying on a bed in a comfortable position. To record muscle sympathetic nerve activity, a tungsten microelectrode with uninsulated tip diameters 1–5 microns (No. 25-05-1, Federick Haer & Co.) was inserted manually through the skin into muscle nerve fibers of the tibial nerve at the popliteal fossa. Spike potentials were amplified (Diamedical DPA-22 and DPA-200) and recorded continuously on magnetic tapes which were later played back into an amplitude analyzer (Diamedical DSE-335P) to convert individual

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**Key words:**
- Baroreflex
- Ganglion blockade
- Genetic predisposition
- Heart rate
- Muscle sympathetic nerve activity

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spikes into uniform pulses. The low-level control of the window discriminator was routinely set to the filter background noise level. Each spike that crossed the low-level generated a normalized voltage step. These normalized voltage steps were integrated to determine the number of the spikes and then the number of individual pulses per minute was counted.

Reflex Cardiovascular and Sympathetic Responses to Phenylephrine

Pressor responses to intravenous injections of phenylephrine (2 μg/kg) through an antecubital venous catheter were consistently accompanied by decreases in both heart rate and muscle sympathetic nerve activity (Fig. 1).

To assess reflex changes in heart rate, a baroreflex slope was calculated by least squares linear regression analysis for each patient. A microcomputer was used to relate each heart interval to the corresponding systolic pressure during the period from the onset of the systolic pressure rising to its peak. The resulting baroreflex slopes for heart intervals were significantly smaller (p < 0.05) in BHT (FH+) (14 ± 2 msec/mmHg) than in either normotensive group (23 ± 2 msec/mmHg in NT (FH−) or 19 ± 3 msec/mmHg in NT (FH+)), but the difference between normotensive groups was not significant.

To assess reflex changes in muscle sympathetic nerve activity, baroreflex slopes were calculated for each patient by relating the percent changes in sympathetic nerve activity to the mean changes in systolic arterial pressures during the corresponding periods for the calculation of baroreflex slopes for heart rate. The resulting baroreflex slopes for muscle sympathetic nerve activity were significantly smaller (p < 0.01) in either group with hypertensive parents (i.e., −8.3 ± 1.0%/mmHg in NT (FH+) or −7.9 ± 0.5%/mmHg in BHT (FH+)) than in NT (FH−) group (−16.3 ± 1.4%/mmHg), but the difference between NT (FH+) and BHT (FH+) groups was not significant.

These results indicate that the adolescents with positive family history of hypertension had significantly reduced reflex inhibition of muscle sympathetic nerve activity even though they remained normotensive. By contrast, reflex bradycardia was reduced in only borderline hypertensive subjects and there was no difference between normotensives whether they had positive family history of hypertension or not. Why the reflex changes only in muscle sympathetic nerve activity (but not in heart rate) was reduced in normotensive subjects with positive family histo-

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ry of hypertension is conjectural. One possible explanation may be due to the difference of either parasympathetic or sympathetic component of baroreflex efferents since the reflex changes in heart rate were almost abolished by intravenous atropine but not in muscle sympathetic nerve activity. This dissociation of baroreflex changes in heart rate from accompanying sympathetic nerve activity has often been reported.

Augmented Depressor Responses to Trimetaphan in Borderline Hypertensive Subjects

As a means of assessing the level of sympathetic vasomotor tone, depressor responses to pharmacological ganglion blockade induced by intravenous injection of trimetaphan (0.05 mg/kg) were also measured at the end of the study. The magnitude of depressor responses was significantly higher (p < 0.05) in BHT (FH+) (19 ± 2 mmHg) than those in normotensive groups with or without positive family history of hypertension (i.e., 14 ± 1 in NT (FH+) or 12 ± 2 in NT (FH−), respectively).

Thus, the elevation of the arterial pressure in BHT (FH+) group was, at least, partly due to the increased sympathetic vasomotor tone.

Conclusion

Our results show that reflex inhibition of muscle sympathetic nerve activity during pressor responses to phenylephrine was reduced in adolescents with positive family history of hypertension even when arterial pressures remained normotensive. Therefore, reduced reflex inhibition of muscle sympathetic nerve activity may represent a genetic predisposition that could eventually lead to development of hypertension by increasing vasomotor tone.

REFERENCES