Reactivity of Arterial Vessels during Antiorthostasis and Systemic Hypotension

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In experiments on rats, changes in blood pressure and cardiac output in response to antiorthostatic (head-down) tilt 15° and 45° were examined under conditions of decreased arterial tone induced by sodium nitroprusside. The decrease in initial systemic blood pressure to 90 mm Hg attenuated the pressor responses to antiorthostasis, while further drop in blood pressure to 70-60 mm Hg provoked depressor responses in half cases. No blood pressure responses to antiorthostasis were observed when blood pressure dropped to 50 mm Hg. Correlation analysis confirmed the existence of a direct dependence of pressor responses to orthostasis on the initial blood pressure.

Key Words: *blood pressure; cardiac output; total peripheral vascular resistance; antiorthostasis*

The antiorthostatic (head-down) hemodynamic reactions are widely used for simulation of hydrostatic shifts in the vascular system during weightlessness [2,3].

We previously showed that spontaneous elevation of blood pressure (BP) is accompanied by clear-cut changes in BP-responses to antiorthostasis [5]. Of importance is the fact that elevation of the initial tone of arterial vessels by infusion of angiotensin II had no effect on compensatory reactions of BP to ortho- and antiorthostasis in rats [6].

Here we examined the effect of BP decrease on the magnitude of antiorthostatic responses. Systemic vasodilation was induced with sodium nitroprusside (SNP), a donor of powerful vasodilator NO.

MATERIALS AND METHODS

Experiments were carried out on heparinized (500 U/kg) mature male Wistar rats weighing 220-340 g. Artificial ventilation was performed with a Vita apparatus. Mean blood pressure (MBP) was recorded in the femoral artery via a PDP-400 transducer. Cardiac output was measured in the ascending aorta with an RKE-2 electromagnetic flowmeter and a 2-mm transducer. The total peripheral resistance (TPR) was calculated as the ratio of MBP to cardiac output in the same time interval.

The antiorthostatic reactions to 15° (n=10) or 45° (n=14) head-down tilt were reproduced as described elsewhere [7].

Infusion of SNP into the femoral vein was performed using an NP-1M peristaltic pump at a rate of 0.25 ml/min. For modeling step-like levels of hypotension, SNP was applied in the following concentrations: 3, 6.2, 12.5, and 25 μg/ml, which reduced BP to 50 mm Hg at most. BP measured immediately before the postural probe was considered as the initial level of BP.

The data were analyzed statistically by Student's t test using routine software. Correlation was determined between BP, TPR, and cardiac output, on the one hand, and initial MBP level, on the other hand. The regression line was calculated using the least square method. The correlation between the above parameters was established according to elongation

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of the correlation field. The correlation coefficient was calculated as described previously [1].

RESULTS

At 15° tilt, the initial MBP and cardiac output were 106.5±2.7 mm Hg and 72.6±7.6 ml/min, respectively (Table 1).

Antiorthostasis significantly increased BP and cardiac output, but had no effect on TPR. SNP could reduce the initial MBP by 15-55 mm Hg. Significant moderation of the pressor responses assessed by MBP and systolic and diastolic BP was observed after the drop of the initial BP to 91.6±2.5 mm Hg, but it was not accompanied by changes in the reactions of cardiac output. The decrease in initial MBP to 71.7±1.3 mm Hg induced depressor responses in 6 of 13 cases (Table 1). As in the above, no changes in the responses of cardiac output to antiorthostasis were observed. In 7 cases, pressor responses were observed, and their magnitudes did not significantly differ from those observed in cases with initial BP of 91.6±2.5 mm Hg. Further decrease in initial BP to 51.6±1.5 mm Hg practically did not affect BP parameters, but was accompanied by insignificant rise of cardiac output and a small decrease of TPR.

Correlation (r) of antiorthostatic effects with the initial level of MAP decreased by SNP infusion (Fig. 1) revealed a linear dependence between the head-down orthostatic reactions and the decrement of initial MBP. High correlation characterized the relationship between initial MBP on the one hand, and systolic (r=0.94±0.06) and diastolic (r=0.96±0.04) reactions, on the other hand. In contrast, correlation between initial MBP and TPR was weaker: r=0.660±0.122. The experiments revealed no significant correlation between initial MBP and cardiac output (r=0.09±0.17). Therefore, only systolic and diastolic pressor reactions

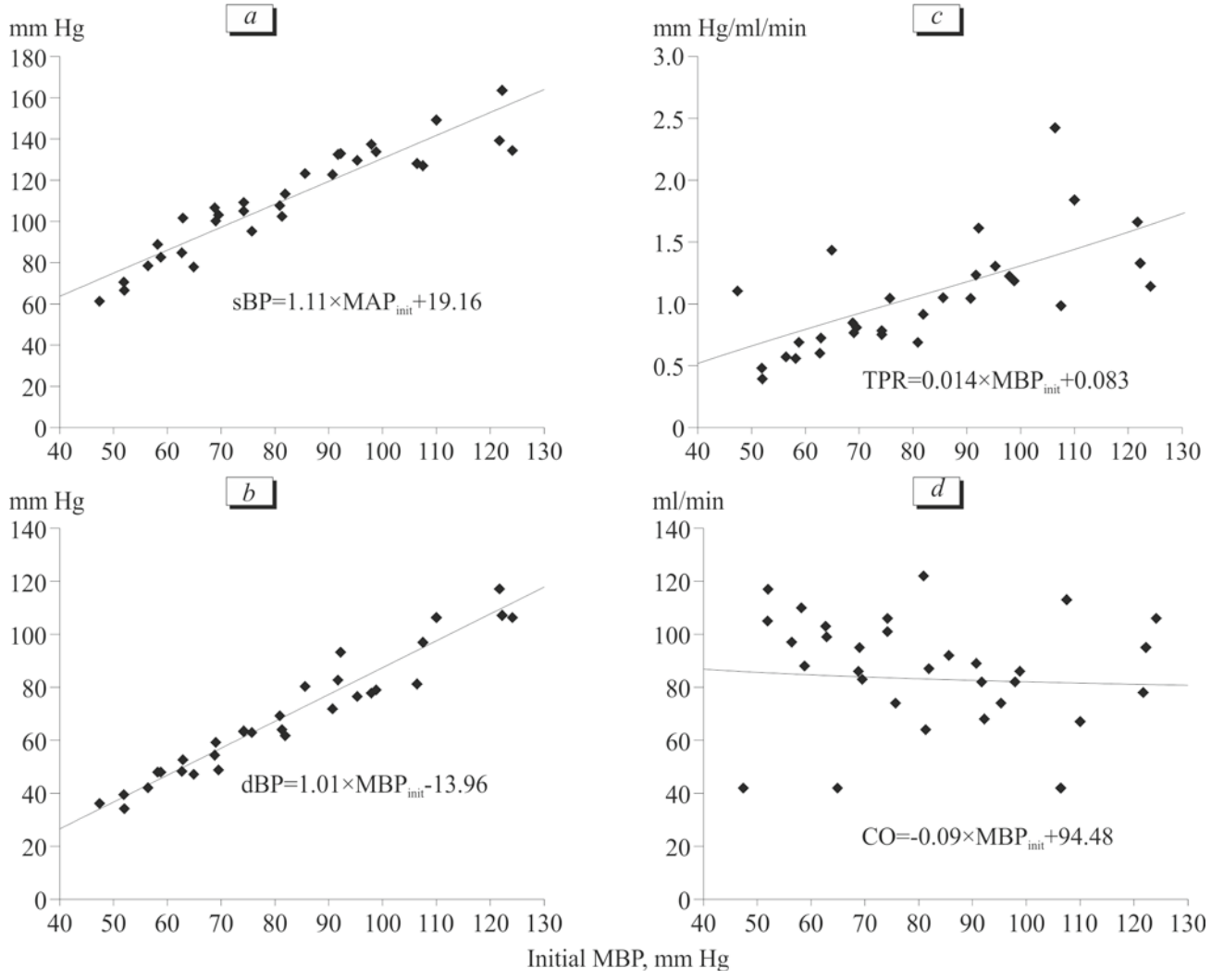

Fig. 1. Effect of initial level of MBP on the antiorthostatic hemodynamic reactions induced by tilt through 15° and assessed by systolic BP (*a*), diastolic BP (*b*), TPR (*c*), and cardiac output (*d*). Here and in Fig. 2: sBP, systolic BP; dBP, diastolic BP; CO, cardiac output.

TABLE 1. Effect of Initial Level of BP in Rats on Hemodynamic Response to Orthostasis by 15° before and during SNP Infusion

Index	Before infusion (122-92)		During infusion (100-80)		During infusion (79-60)		During infusion (79-60)		During infusion (<60)	
	initial value	magnitude of reaction (*n*=10)	initial value	magnitude of reaction (*n*=7)	initial value	magnitude of reaction (pressor responses, *n*=7)	initial value	vagnitude of reaction (depressor responses, *n*=6)	initial value	magnitude of reaction (*n*=6)
MBP, mm Hg	106.5±2.75	8.99±2.27	91.6±2.47	4.7±1.47**	71.7±1.91	5.31±0.95**	66.2±2.05	-4.4±1.67***	51.6±1.46	-3.1±0.95***
Systolic BP, mm Hg	125.8±1.24	15.69±5.24	121.3±4.35	5.44±1.65***	98.5±2.22	6.87±1.29***	90.8±4.21	-6.27±2.29***	71.1±4.09	-2.75±2.12***
Diastolic BP, mm Hg	91.3±3.43	8.13±2.51	73.2±1.5	3.6±1.38**	5.96±1.84	3.79±0.59**	51.5±1.76	-3.63±1.3***	40.2±0.7	-2.97±0.81***
TPR, mm Hg/ml/min	1.61±0.16	-0.03±0.03	1.15±0.08	-0.04±0.2	0.94±0.11	-0.01±0.02	0.97±0.17	-0.1±0.03	0.65±0.13	-0.08±0.02
Cardiac output, ml/min	72.6±7.6	7.0±0.75	81.9±4.75	7.71±1.98	80.4±5.56	7.43±2.04	78.5±12.46	-3.17±2.36*	88.4±12.53	4.2±0.73

Note. Here and in Tables 2: *p<0.05, **p<0.01, ***p<0.001 compared to the corresponding values before infusion. The range of initial MBP values is shown in parentheses.

TABLE 2. Effect of Initial Level of BP in Rats on Hemodynamic Response to Orthostasis by 45° before and during SNP Infusion

Index	Before infusion (115-82)		During infusion (77-60)		During infusion (77-60)		During infusion (<60)	
	initial value	magnitude of reaction (*n*=14)	initial value	magnitude of reaction (pressor responses, *n*=7)	initial value	magnitude of re-actions (depressor responses, *n*=9)	initial value	magnitude of reaction (*n*=10)
MBP, mm Hg	98.7±3.96	10.44±2.19	70.8±2.32	7.43±2.49**	67.3±1.31	-5.78±1.24***	56.1±1.77	-3.5±1.44***
Systolic BP, mm Hg	114.8±5.53	11.67±1.83	82.1±6.88	8.26±2.67**	79.8±3.07	-5.8±1.44***	71.7±3.4	-3.42±1.63***
Diastolic BP, mm Hg	84.5±3.85	8.71±2.44	61.27±2.78	6.46±2.29**	56.9±2.7	-5.82±1.1***	44.6±2.23	-4.02±1.17***
TPR, mm Hg/ml/min	1.27±0.1	-0.06±0.02	1.1±0.13	-0.09±0.03	0.97±0.11	-0.16±0.02	0.91±0.11	-0.2±0.05
Cardiac output, ml/min	83.8±6.23	12.85±1.51	71.0±8.59	13.17±1.85	76.2±7.08	7.0±1.72	64.7±5.19	11.88±4.45

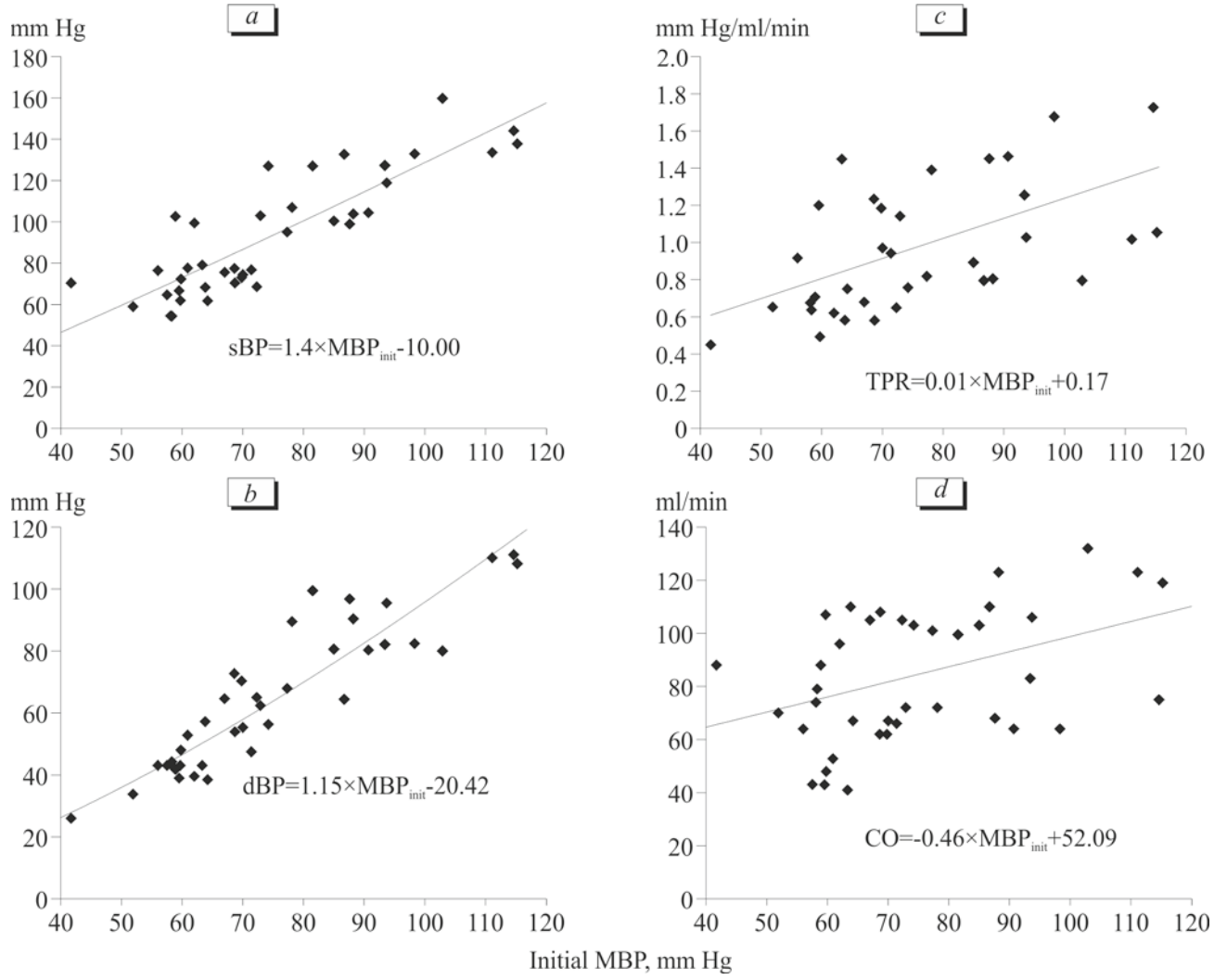

Fig. 2. Effect of initial level of MBP on the antiorthostatic hemodynamic reactions induced by tilt through 45° and assessed by systolic BP (*a*), diastolic BP (*b*), TPR (*c*), and cardiac output (*d*).

and changes in TPR caused by head-down tilt depended on the initial MBP, but not on cardiac output. Thus, the above parameters describing vascular responses to antiorthostasis can serve as the indices for evaluation of reactivity of the arterial system.

Thus, comparison of the antiorthostatic effects induced by a 15° tilt during SNP-provoked hypotension of various degree and correlation analysis of the related parameters indicate progressive moderation of these effects during persistent infusion.

In the antiorthostatic experiments with 45° tilt, the initial MBP and cardiac output were 98.7±4.0 mm Hg and 83.6±6.2 ml/min, respectively. Here, the head-down tilt elevated all BP indices and increased cardiac output, but decreased TPR (Table 2).

Moreover, the 45° tilt experiments revealed moderation of the pressor reaction of MBP and pressor responses of systolic and diastolic BP during infusion of SNP. Similar to 15° tilt, the drop of MBP to 67.3±1.3 mm Hg in 45° tilt experiments resulted in a decrease of pressor responses (in 7 of 16 cases) and appearance of depressor ones in 9 of 16 cases (Table 2). Moreover, pressor responses during SNP infusion were significantly less pronounced than before it. Further decrease in initial MBP below 60 mm Hg (56.1±1.8 mm Hg) was accompanied by only a slight decrease in BP indices and TPR value, but led to elevation of cardiac output.

Correlation analysis of the dependence of antiorthostatic effects on the level of initial MBP revealed linear relationships between these values (Fig. 2). The correlation was high for MBP (r=0.94±0.05), systolic (r=0.86±0.07) and diastolic (r=0.89±0.07) BP, moderate for TPR (r=0.55±0.12) and weak for cardiac output (r=0.36±0.14).

In contrast to the effect of 15° tilt antiorthostasis, the correlation analysis of 45° tilt revealed a linear dependence on the initial level of MBP not only for BP indices and TPR, but also for cardiac output, although it less strictly depended on the initial MBP compared

to the above indices. Therefore, while the initial level of MBP predominantly modulated the vascular effects of the antiorthostasis, its effect on cardiac output cannot be excluded. We previously showed that 15° head-down tilt produced no effect on systolic BP in the left ventricle, while 45° tilt increased it [7].

In this study, we used systemic vasodilation caused by SNP. Being a NO donor, this agent decreased myogenic vascular tone. Probably, this mechanism of reduction of the myogenic tone of arterial vessels is crucial for manifestation of the dependence between the effects of antiorthostasis and the initial level of arterial tone during hypotension. The involvement of NO in the postural reactions [11] including the antiorthostatic ones was previously demonstrated [12].

We found a linear dependence of the pressor reactions to antiorthostasis on initial MBP level. The greatest pressor responses were observed at the near-normal initial MBP (90-110 mm Hg in narcotized rats). The same range of initial MBP corresponded to maximal reactions of arterial vessels during orthostasis [10] or vasomotor effects of phenylephrine [8].

These findings suggest that the decrease in baseline (initial) BP with SNP below the physiological range (80-110 mm Hg in rats [4]) diminishes the constriction reserve, which agrees with the hypothesis proposed on the basis of experiments with phenylephrine [9]. Moreover, the corresponding dependence is linear.

The data also attest to significant role played by the initial state of vascular system in shaping its reactivity. It is clearly demonstrated by the character of correlation and opposite directivity of the vascular reactions developed after delevation of initial BP to various ranges. To a certain degree, this study corroborates Wilder's law of initial value [13], which suggests the dependence of changes in activity indices of a functional system induced by some perturbations on their initial level.

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