Parameters of Microcirculation in Paired Formations after Single Aspirin Administration: Laser Doppler Flowmetry Data

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Laser Doppler flowmetry showed that aspirin can induce blood flow reduction and transitory manifold increase or decrease in vascular tone in rat skin and kidneys. The dynamics is more illustrative when parameters of individual animals are evaluated and depends on the areas of blood flow recording. Deaths and reduction of narcotic sleep duration were noted in concomitant use of nembutal and aspirin.

Key Words: *blood flow; vascular tone; skin; kidney; aspirin; laser Doppler flowmetry*

Aspirin (acetylsalicylic acid) is now traditionally used in complex therapy as an antithrombotic agent irreversibly blocking cyclooxygenase activity and is recommended as a drug with beneficial effect on hemorheological status in cardiovascular patients [1]. It is also common practice to use aspirin in preventive treatment of recurrent infarctions [5,6]. Effects of salicylic acid derivatives on vascular system are not clearly understood. According to Kernogan index [4], a trend towards the increase in vascular tone, *e.g.* on intraorgan vessels, is observed after course treatment with aspirin. Here we studied possible effects of aspirin on blood flow and vascular tone in paired fragments of microvascular bed (MVB) in rat skin and kidney using laser Doppler flowmetry (LDF).

MATERIALS AND METHODS

Experiments were carried out on rats weighed 200-210 g under nembutal anesthesia (5 mg/100 g body weight, intraperitoneally). Aspirin water solution was administered intramuscularly 0.5 mg/100 g body weight. Capillary blood flow was measured using LDF approach with a LAKK-01 (LAZMA) flowmeter. Microcirculation parameters (MP) expressed in conventional units were registered with 10 Hz sample rate before and during 1 h after agent administration (recording time at least 2 min). Areas of blood flow registration: symmetric MVB sites in the skin (frontal, temporal, auricular and abdomen area) and kidneys. Dopplerograms were processed by conventional spectral analysis. Frequency range in periodograms was determined by MP sample rate and was 0-5 Hz. For the analysis of MVB vascular tone spectrum, the frequency components were analyzed in the range of 0.009-0.020 Hz, where according to current views, the frequency components carry information concerning the involvement of the endothelial factor in the regulation of muscle tone determined by the NO activity; 0.02-0.20 Hz, low-frequency (LF), where frequency components in the range of 0.02-0.06 Hz may be regarded as a reflection of neurogenic (LFn) effects, and in the range of 0.06-0.20 Hz corresponding to myogenic effects (LFm). Frequency components in the range of 0.2-5.0 Hz reflecting high-frequency fluctuations, cardiac and respiratory rhythm, were not analysed in this study. The impact of endothelial (VtoneE), neurogenic (VtoneN), and myogenic (VtoneM) mechanisms in vascular tone was assessed according to ratio σ/ALF, where σ is

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mean-square deviation (MSD) and ALF is maximal amplitude of low-frequency components in the specified frequencies rage, as presently accepted [3]. The data are presented for MVB fragments of symmetrical areas and symmetrical fragments of homonymous organs of individual animals.

The data were processed using Statistica 6.0 software.

RESULTS

Mean MP values and vascular tone parameters for areas of the left (Table 1) and right (Table 2) sides are presented.

Changes in MVB parameters at the left side after aspirin administration were statistically insignificant. On the right side, the decrease in MP and endothelial component of muscle tone was significant (Tables 1, 2). The increase in mean-square deviation indicated nonuniformity of vascular reaction in different regions in response to aspirin administration, which was most clearly seen as early as 20-30 min after administration.

Average values are based upon individual cases, which description provides more realistic view of the adaptation features against the background of exposure to aspirin. Experimental animals, similarly to humans, exhibit individual peculiarities of blood flow fluctuations and different baseline MVB parameters, what defines the dynamics. Baseline MP values and endothelial, neurogenic, and myogenic components of the vascular tone are presented for symmetric MVB fragments of the skin in certain individual cases (Table 3), as well as changes in these parameters 30 and 60 min after aspirin administration (Fig. 1 and 2). Original records of the blood flow (dopplerograms) indicated that blood flow reduction to 50% from the baseline may appear in certain areas (more often at the right side) after aspirin administration (Fig. 1).

Endothelial component of vascular tone increased 3-9-fold 20-30 min after intramuscular aspirin administration (Fig. 2). However, reduction in endothelial

TABLE 1. Changes in MVB Parameters on the Left Side after Aspirin Administration ($M \pm m$)

Parameters	Phase		
	baseline	aspirin (30 min)	aspirin (more than 1 h)
MP, arb. units	14.942±2.280	13.772±3.687	13.702±2.858
σ	1.084±0.306	1.125±0.420	1.065±0.333
σ/Ae	0.052±0.039	0.049±0.040	0.032±0.015
σ/An	0.049±0.042	0.044±0.035	0.043±0.070
σ/Am	0.042±0.026	0.040±0.027	0.060±0.032
n	11	11	11

Note. Here and in Table 2: amplitudes of endothelial (Ae), neurogenic (An), and myogenic (Am) frequency components.

TABLE 2. Changes in MVB Parameters on the Right Side after Aspirin Administration ($M \pm m$)

Parameters	Phase		
	baseline	aspirin (30 min)	aspirin (more than 1 h)
MP, arb. units	15.296±3.638	13.95±3.033	10.427±2.251**
σ	1.151±0.287	1.325±0.490*	1.181±0.334
σ/Ae	0.172±0.156	0.165±0.309*	0.048±0.032**
σ/An	0.042±0.019	0.059±0.048*	0.044±0.024
σ/Am	0.038±0.020	0.046±0.040*	0.046±0.029
n	11	11	11

Note. *$p<0.05$ (F-test), **$p<0.01$ (t-test) in comparison with baseline values.

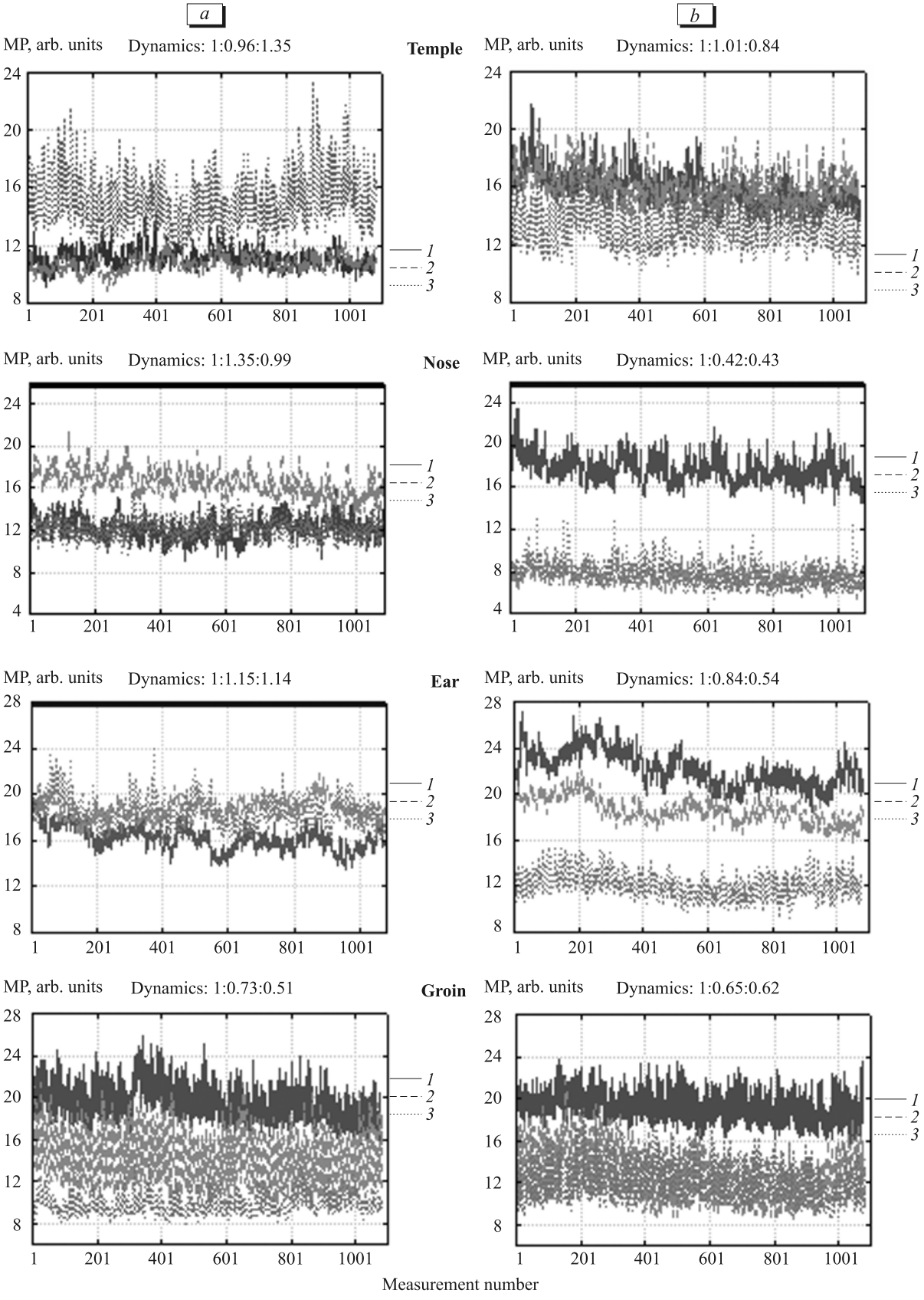

Fig. 1. Dopplerograms for symmetric skin areas against the background of exposure to aspirin at the baseline (*1*) and 30 (*2*) and 60 min (*3*) after drug administration. *a*) on the left side, *b*) on the right side.

vascular tone was also apparent (for temporal and abdomen vessels). The increase in myogenic tone was observed for temporal, nasal and auricular vessels at the right side. The most pronounced rise of neurogenic component was observed for nasal MVB.

Pronounced changes in vascular tone were also observed in the visceral organs. MP, MSD, and tonus components were changed in rat kidneys against the

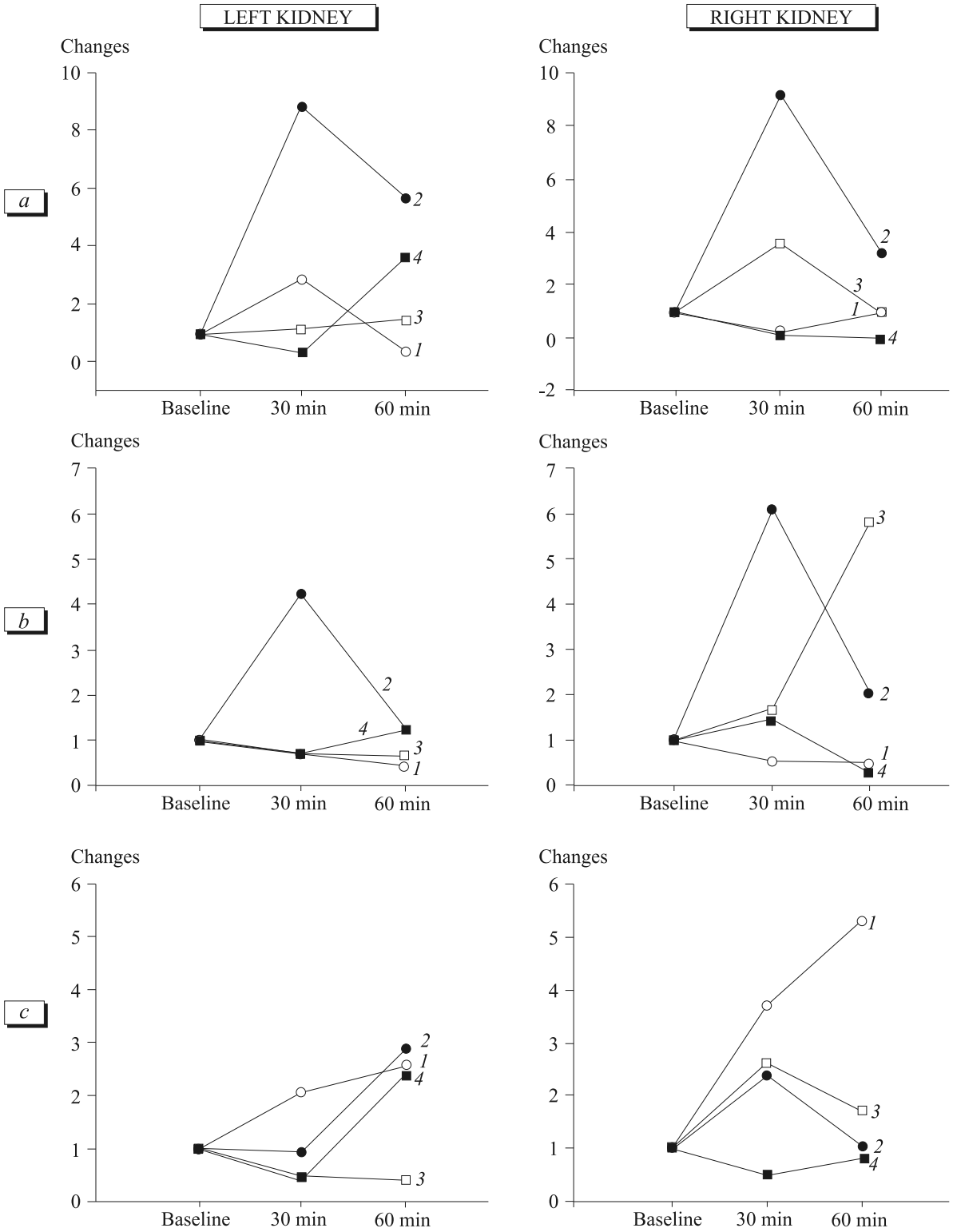

Fig. 2. Assessment of vascular tone components for rat skin fragments during 1 h after aspirin administration compared to baseline values. *a*) VtoneE changes; *b*) VtoneN changes; *c*) VtoneM changes. *1*) temple; *2*) nose; *3*) ear; *4*) groin.

background of aspirin treatment (multiple blood flow measurements during one hour after drug administration; Fig. 3).

The changes were also obvious in the dynamics of the state: changes in MP and MSD on the left side, and mild changes in MP and rise in variability on the right side. In the dynamics of vascular tone components, the increase in myogenic and endothelial components was

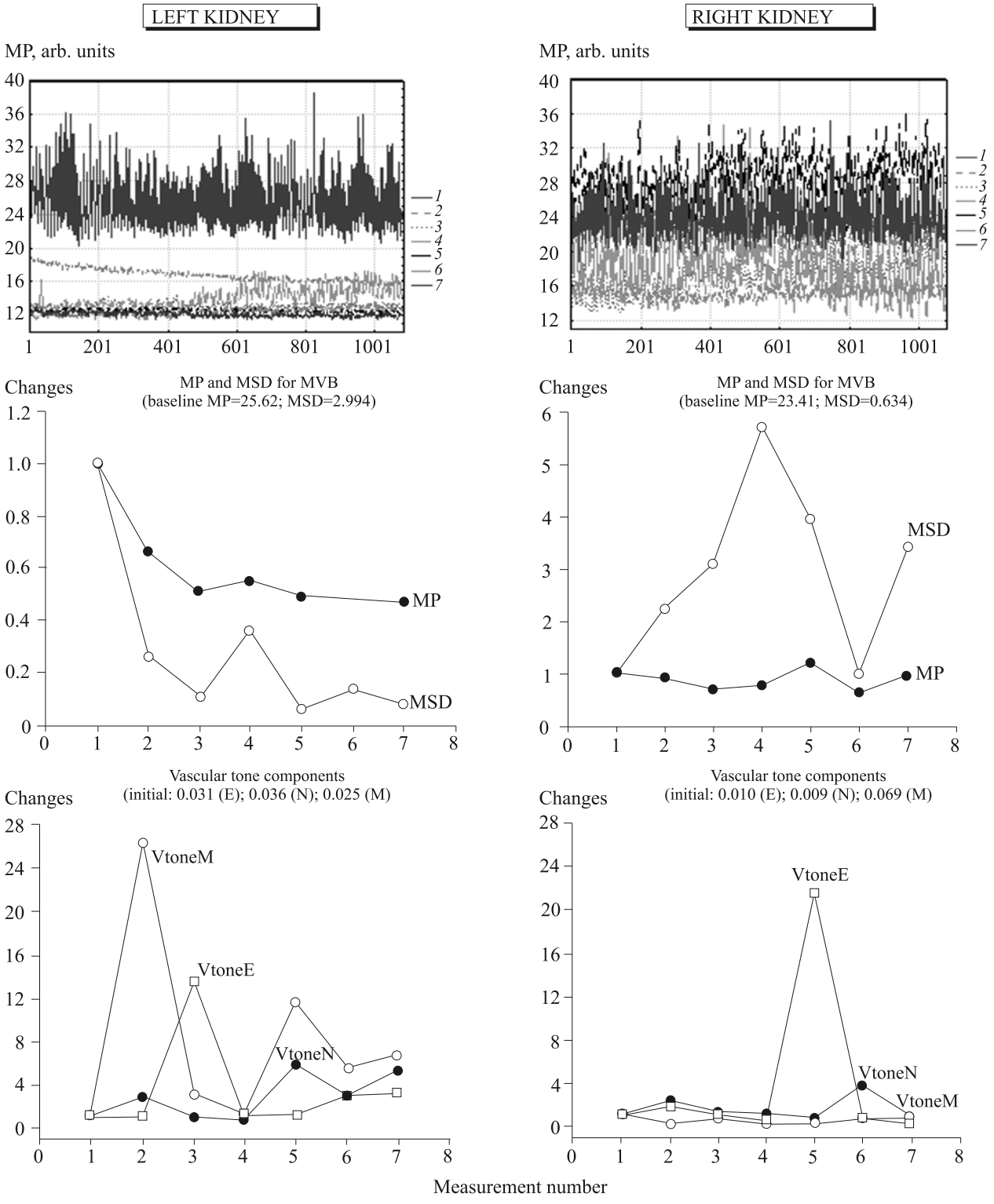

Fig. 3. Changes in MVB parameters in rat kidney over 1 h after aspirin administration compared to baseline values. *1*) baseline; *2-7*) successive measurements during the hour.

TABLE 3. Baseline MVB Values for Individual Cases (*M*±*m*)

Area	MP, arb. units and tone components	
	on the left side	on the right side
Temple	11.140±0.676	15.880±1.315
	0.018 (e), 0.035 (n), 0.011 (m)	0.066 (e), 0.036 (n), 0.010 (m)
Nose	12.160±1.063	17.710±1.326
	0.008 (e), 0.022 (n), 0.027 (m)	0.036 (e), 0.025 (n), 0.018 (m)
Ear	16.200±1.019	22.200±1.562
	0.015 (e), 0.006 (n), 0.070 (m)	0.010 (e), 0.006 (n), 0.036 (m)
Groin	19.360±1.806	19.130±1.501
	0.023 (e), 0.011 (n), 0.044 (m)	0.593 (e), 0.055 (n), 0.066 (m)

Note. e: endothelial, n: neurogenic, m: myogenic.

more pronounced in the left kidney and the increase in the endothelial component in the right kidney. In some animals, inverse dynamics was observed, which suggests that differentiated approach to investigation of the reactions to the drugs is needed in animals with different right-left orientation.

It should be noted, that two forms of MVB transition into the new state were noted in MP dynamics in different MVB sites of the skin and kidneys against the background of aspirin treatment: "jump" and "continuity". Similar forms of transitions were previously shown in our studies for the conditions of inflammation development, systemic blood pressure development, *etc*. One may assume that the type of transition is determined by different sensitivity to aspirin in arterial and venous vessels. Dramatic changes in MP and vascular tone in certain regions may cause blood flow disturbances. The latter suggests that in the analysis of the effects of pharmacological drug one should choose the most vulnerable regions, like in cosmic medicine in life-support and survival system development [2].

Interestingly, that there were lethal cases after anesthetic drug supplementation against the background of aspirin exposure (it can be hypothesized that the combination of anesthetic drug and aspirin caused lung vessel spasm). Similar outcome was also observed after intraperitoneal administration. In one animal, a decrease in narcotic sleep duration was noted: few minutes after aspirin administration the rat woke up and abandoned the place of the experiment. These individual cases prove that aspirin in combination with other drugs may lead to an unexpected result.

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