Changes of Adrenaline Concentration in Various Organs of the Rat during and Following Four Hours' Swimming

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Abstract: Changes in the concentrations of adrenaline and noradrenaline in various organs of the rat were examined during and following four hours' swimming in 25°C water. During the period of swimming, the adrenaline concentration increased time-dependently in the heart, spleen, kidney, liver, lung, abdominal wall muscle and thigh muscle, whereas the noradrenaline concentration tended to decrease. Three hours after the end of swimming, adrenaline concentrations in the peripheral organs were reduced, but were still higher than those of the control group. The adrenaline value returned to normal within 24 hours. From these results, adrenaline concentrations in the heart and various other peripheral organs are considered to increase gradually with the duration of swimming and to be considerably high for at least several hours after the cessation of swimming.

Key words: Swimming—Adrenaline—Noradrenaline—Rats—Organs—Urine—Stress

INTRODUCTION

Adrenaline is present in blood and urine. Plasma level and urinary excretion of adrenaline are increased under various stressful conditions,^{1,2)} due to enhanced release of adrenaline from the adrenal medulla.^{3,4)}

It is known that a small amount of adrenaline is contained in various organs of mammals.⁵⁾ Previous observations by several workers⁶⁻⁸⁾ have shown that swimming induces an increase in adrenaline concentrations in various peripheral organs of the rat. An increase in adrenaline has also been reported in mammalian organs after hemorrhage,^{9,10)} administration of insulin^{8,11)} or another drug,¹²⁾ and stimulation of the splanchnic nerve or ventromedial hypothalamus.^{11,13)} It was demonstrated that the site of swimming-induced increases in adrenaline is likely to be sympathetic nerve endings,⁶⁾ suggesting that adrenaline is involved in sympathetic neurotransmission under stressful situations.

From the standpoint of stress physiology, it seems to be important to study more precisely changes in adrenaline in organs during stress. The aim of this study was to investigate the time course of changes in adrenaline concentration

in rat organs during and following swimming. Several experiments were performed for this purpose.

MATERIALS AND METHODS

Animals:

Male Sprague-Dawley rats (Clea, Japan) were kept on 12-hour light-dark cycles for at least one week before the swimming exercise. Food and water were given *ad libitum*. The ambient temperature and humidity were controlled at $25 \pm 1^\circ\text{C}$ and $55 \pm 5\%$, respectively.

Swimming:

The rats were placed individually in polyethylene buckets (50 cm i.d. and 60 cm in height) containing 50 cm of water, for various periods of time. The temperature of the water was maintained between 25 and 28°C . The swimming experiment was performed during the dark phase of the cycle to minimize sleep deprivation during the swimming exercise. Urine, blood and organs were obtained as described below.

Sampling of urine, blood and organs:

After the period of swimming was completed, blood and organs of the rats were obtained under urethane-chloralose anaesthesia,⁽⁶⁾ unless otherwise noted.

For urine collection, the rats were individually housed in metabolic cages (Shinano Seisakusho, Tokyo) and 5-, 19- or 24-hour urine was collected in a glass bottle containing 1 N H_2SO_4 . Urine samples were stored in a refrigerator (4°C) until analysis.

Measurement of adrenaline and noradrenaline in biological materials:

Catecholamines in urine were purified by alumina adsorption, and the acidic extract was injected into a high-performance liquid chromatograph using a Nucleosil-5SA column (Macherey-Nagel, Chemcopak, 4×200 mm) eluted with 0.1 M NaH_2PO_4 containing 10% methanol. Adrenaline and noradrenaline concentrations in the effluent were continuously determined by the trihydroxyindole method.

Catecholamines in plasma and organs were analyzed as described previously.⁽⁶⁾

Statistical analysis:

Catecholamine contents of organs were expressed as nmol or pmol per g wet tissue, unless otherwise stated, and plasma levels were expressed as pmol/ml. Urinary excretion of adrenaline and noradrenaline was presented as pmol/mg of creatinine. The significance of the data was evaluated with the two tailed t-test.

RESULTS

1) Changes in adrenaline and noradrenaline concentrations in plasma and various organs of the rats during four hours' swimming

Fig. 1. Adrenaline and noradrenaline concentrations in the heart of rats after various periods of swimming.

C: Control, S.3: 20-min swim, S1: 1-hour swim, S2: 2-hour swim, and S4: 4-hour swim. See footnote to Table 1.

Figure 1 shows adrenaline and noradrenaline concentrations in the rat heart immediately after 0.3, 1, 2 and 4 hours of swimming. A time-dependent increase in adrenaline concentration and a time-dependent decrease in noradrenaline concentration were observed during swimming. After four hours' of swimming, an approximately eight-fold increase was found in the adrenaline content of the heart. It is interesting that a significant increase in the adrenaline content of the heart was recognized after only one-hour of swimming ($p < 0.01$).

A time-related increase in adrenaline concentration was also observed in the spleen, liver, kidney, abdominal wall muscle and thigh muscle. Plasma levels of adrenaline and noradrenaline were increased after 1, 2 and 4 hours of swimming (Table 1). On the contrary, a marked decrease in adrenaline concentration was found in the adrenal gland after swimming. Adrenaline contents of the hypothalamus and pons-medulla also decreased time dependently during swimming.

2) Adrenaline and noradrenaline concentrations in rat plasma and organs immediately after and three hours after four hours of swimming

Recovery of swimming-induced changes in adrenaline and noradrenaline concentrations in plasma and organs of the rats is shown in Table 2. After the cessation of the 4-hour swim, the adrenaline level of the heart returned toward normal, but three hours later, the value was still higher than that of the control group ($p < 0.01$). Similar results were obtained for the spleen, kidney, abdominal wall muscle and thigh muscle. Noradrenaline in the peripheral organs was almost restored within three hours after swimming, but the levels in the heart and lung

Table 1. Adrenaline and noradrenaline concentrations in various organs of rats after 0.3, 1, 2 and 4 hours of swimming

	Control	Duration of swimming (hour)			
	[6]	0.3 [6]	1 [6]	2 [6]	4 [6]
Spleen					
Adrenaline	34.4 ± 3.5	29.9 ± 3.9	44.5 ± 5.2	71.2 ± 3.9**	85.7 ± 7.1**
Noradrenaline	6.16 ± 0.62	5.32 ± 0.81	6.07 ± 0.58	5.86 ± 0.36	4.52 ± 0.42*
Kidney					
Adrenaline	12.1 ± 2.9	20.2 ± 3.7	37.7 ± 5.7**	68.2 ± 2.6**	69.0 ± 6.0**
Noradrenaline	1.010 ± 0.112	0.704 ± 0.101	0.995 ± 0.070	0.857 ± 0.045	0.962 ± 0.096
Liver					
Adrenaline	1.56 ± 0.16	1.78 ± 0.17	3.01 ± 0.47*	7.67 ± 0.92**	12.42 ± 1.02**
Noradrenaline	0.379 ± 0.033	0.417 ± 0.028	0.410 ± 0.024	0.407 ± 0.034	0.347 ± 0.036
Lung					
Adrenaline	4.64 ± 1.08	9.91 ± 1.30*	22.49 ± 7.55*	23.82 ± 4.37**	28.80 ± 1.18**
Noradrenaline	0.605 ± 0.045	0.515 ± 0.016	0.496 ± 0.027	0.418 ± 0.079	0.428 ± 0.020**
Abdominal wall muscle					
Adrenaline	2.68 ± 0.53	3.57 ± 0.42	7.90 ± 1.14**	15.93 ± 1.65**	21.44 ± 1.85**
Noradrenaline	0.306 ± 0.020	0.282 ± 0.029	0.286 ± 0.024	0.324 ± 0.024	0.285 ± 0.011
Thigh muscle					
Adrenaline	2.28 ± 0.34	3.18 ± 0.25	6.72 ± 0.70**	15.45 ± 1.67**	21.48 ± 1.59**
Noradrenaline	0.424 ± 0.016	0.392 ± 0.010	0.407 ± 0.013	0.394 ± 0.028	0.338 ± 0.010**
Adrenal gland (nmol/pair)					
Adrenaline	167.6 ± 5.6	170.9 ± 6.1	143.2 ± 6.4*	122.9 ± 4.2**	84.2 ± 6.3**
Noradrenaline	38.6 ± 1.9	29.1 ± 1.9**	36.5 ± 3.2	31.7 ± 2.2*	29.2 ± 2.0**
Plasma (pmol/ml)					
Adrenaline	1.9 ± 0.4	10.5 ± 4.0	14.6 ± 2.5**	25.0 ± 3.0**	25.0 ± 5.3**
Noradrenaline	1.6 ± 0.1	7.1 ± 1.8*	12.0 ± 2.2**	11.0 ± 0.6**	8.8 ± 1.2**
Hypothalamus					
Adrenaline	172.3 ± 8.4	168.0 ± 14.7	129.8 ± 8.8**	109.5 ± 6.2**	84.3 ± 3.2**
Noradrenaline	8.71 ± 0.50	7.59 ± 0.30	6.51 ± 0.17**	6.25 ± 0.33**	5.73 ± 0.27**
Pons-medulla					
Adrenaline	33.0 ± 2.8	29.4 ± 2.6	26.2 ± 1.9	24.5 ± 1.1*	21.6 ± 1.0**
Noradrenaline	2.77 ± 0.10	2.67 ± 0.10	2.46 ± 0.10	2.49 ± 0.14	2.30 ± 0.06**

Twelve-week-old rats, weighing from 320 to 500 g, were used. Immediately after swimming, biological samples were taken under urethane-chloralose anaesthesia. Numbers of observations are given in brackets and values are mean and S.E., expressed as pmol/g wet tissue for adrenaline and as nmol/g wet tissue for noradrenaline, unless otherwise noted. *: $p < 0.05$ and **: $p < 0.01$, for swimming group vs. control group. Results for four hours' swimming were partially presented in a previous paper.⁶⁾

Table 2. Adrenaline and noradrenaline concentrations in various organs of rats immediately after and three hours after swimming

	Control [10]	After swimming (hour)	
		0 [6]	3 [6]
Heart			
Adrenaline	52.0±3.4	314.0±54.7**	100.1±13.2**
Noradrenaline	5.74±0.42	2.96±0.24**	3.61±0.14**
Spleen			
Adrenaline	33.9±2.4	114.0±16.3**	83.4±10.2**
Noradrenaline	6.02±0.55	5.66±0.70	6.80±0.82
Kidney			
Adrenaline	3.34±0.81	46.58±9.79**	16.67±2.50**
Noradrenaline	0.765±0.035	0.735±0.045	0.779±0.050
Liver			
Adrenaline	1.45±0.25	15.30±1.86**	5.94±1.02**
Noradrenaline	0.459±0.014	0.365±0.016**	0.440±0.034
Lung			
Adrenaline	5.3±1.2	31.6±2.4**	16.3±1.8**
Noradrenaline	0.656±0.032	0.475±0.029**	0.558±0.012*
Abdominal wall muscle			
Adrenaline	1.68±0.13	23.72±2.75**	8.47±1.22**
Noradrenaline	0.319±0.024	0.301±0.031	0.296±0.028
Thigh muscle			
Adrenaline	1.80±0.17	32.86±3.30**	13.63±2.22**
Noradrenaline	0.555±0.017	0.476±0.038	0.515±0.031
Adrenal gland (nmol/pair)			
Adrenaline	157.1±4.4	84.2±4.8**	74.5±4.0**
Noradrenaline	33.4±2.4	31.6±2.8	31.0±2.3
Plasma (pmol/ml)			
Adrenaline	1.0±0.3	4.7±1.0**	3.7±1.1*
Hypothalamus			
Adrenaline	195.1±4.6	89.6±6.5**	71.5±3.4**
Noradrenaline	9.41±0.33	6.22±0.20**	7.88±0.2**
Pons-medulla			
Adrenaline	30.3±0.6	19.5±0.8**	22.0±1.1**
Noradrenaline	2.66±0.09	2.31±0.04*	2.80±0.07

Twelve-week-old rats, 380 to 440 g, were used. Immediately after and 3 hours after the cessation of four hours of swimming, blood and organs were taken under sodium pentobarbital anaesthesia. See footnote to Table 1.

were still lower than those of the control.

The plasma level of adrenaline in the swimming group 3 hours after swimming was higher than that of the control ($p<0.05$). No recovery of adrenaline concentration was observed in the adrenal gland or in the brain regions examined.

3) Adrenaline and noradrenaline concentrations in rat heart and brain, 0, 24 and 72 hours after four hours of swimming

Twenty-four and 72 hours after four hours' swimming, adrenaline content of

the heart in the swimming group did not differ significantly from that of the control group, as seen in Table 3. The data showed no significant difference in noradrenaline content between the two groups. Therefore, the increased level of adrenaline and the decreased level of noradrenaline produced by swimming were considered to have returned to normal within 24 hours.

The adrenaline level in the pons-medulla of the swimming group was significantly higher than that of the control group 24 hours after swimming, but the difference

Table 3. Adrenaline and noradrenaline concentrations in the heart and brain regions of rats after swimming

	After swimming (hour)					
	0 Control [6]	Swimming [6]	24 Control [6]	Swimming [6]	72 Control [6]	Swimming [6]
Heart						
Adrenaline	89.4 ±9.8	324.4 ±56.0**	114.7 ±32.4	125.9 ±22.7	103.6 ±17.5	165.9 ±59.2
Noradrenaline	4.16 ±0.36	2.95 ±0.28*	4.53 ±0.58	3.66 ±0.39	4.54 ±0.57	3.98 ±0.42
Hypothalamus						
Adrenaline	191 ±14	98 ±10**	176 ±10	155 ±5	184 ±6	180 ±18
Noradrenaline	9.83 ±0.59	6.96 ±0.50**	9.41 ±0.37	10.09 ±0.32	10.06 ±0.25	9.47 ±0.56
Pons-medulla						
Adrenaline	26.4 ±1.3	21.3 ±1.4*	30.6 ±1.2	39.5 ±2.1**	30.2 ±1.0	34.4 ±2.3
Noradrenaline	3.08 ±0.08	2.74 ±0.08*	2.96 ±0.11	3.27 ±0.13	3.27 ±0.07	3.33 ±0.10

Eleven- to 23-week-old rats, 250–600 g, were used. Immediately after, 24 or 72 hours after the cessation of four hours of swimming, organs were removed after decapitation. See footnote to Table 1.

Table 4. Urinary excretion of adrenaline and noradrenaline in rats before and after swimming

	3 days before swimming	After swimming		
		1st day	2nd day	5th day
Adrenaline excretion				
Control group [7]	59±15	91±17	87±11	69±9
Swimming group [5]	63±12	1675±536**	158±21**	86±12
Noradrenaline excretion				
Control group [7]	765±35	528±38	544±25	464±31
Swimming group [5]	745±36	2479±446**	565±46	501±33

Seven-week-old rats, 220–260 g, were used. Five-hour urine (15:30–20:30) was collected immediately after the end of 3.5 hours of swimming (12:00–15:30). The urine (15:30–20:30) was also obtained 3 days before swimming and on the 2nd and 5th days after swimming. Values are the mean and S.E., expressed as pmol/mg creatinine. Numbers of observations are given in brackets. **: $p < 0.01$ for swimming group vs. control group.

was not recognized after 72 hours. No group difference was observed in the noradrenaline levels either 24 hours after or 72 hours after swimming.

4) *Urinary excretion of adrenaline and noradrenaline in the rats before and after 3.5 hours of swimming*

In order to obtain further evidence supporting swimming-induced increases

Fig. 2. Changes in urinary excretion of adrenaline and noradrenaline in rats before and after 3.5 hours of swimming.

Seven-week-old rats weighing 220 to 260 g were exposed to 3.5 hours of swimming and 24-hour urine was collected. The results shown are means and S.E. from 5 swimming-exposed (open circles) and 7 control rats (closed circles). **: $p < 0.01$, *: $p < 0.05$ compared with the values of the control group on the same day.

in plasma levels of adrenaline and noradrenaline, urinary excretion of the two amines was measured before and after 3.5 hours of swimming (Fig. 2). The swimming caused a marked increase in catecholamine excretion, especially in adrenaline excretion, in the rats. A 26-fold increase in adrenaline value was observed in the urine samples obtained during the five hours immediately after swimming (Table 4). On the second day, the adrenaline value of the swimming group was still higher than that of the control, but this was not the case on the fifth day.

DISCUSSION

It has been reported that small amounts of adrenaline are contained in various mammalian organs.^{3,5,6,8,9,12,14-18)} Published data on the organ contents of adrenaline, however, show a large variability (Table 5). Recently, it has become possible to measure a minute amount of adrenaline in the presence of noradrenaline using high-performance liquid chromatography (HPLC) coupled with fluorometric or electrochemical detection, and adrenaline levels in the organs studied tend to lower. In the present study, adrenaline was determined by HPLC, and adrenaline content of the heart was found to be about 1–2% of noradrenaline in the rats in a basal condition, a result which is in good accordance with the values reported recently.^{3,18)} Our data on adrenaline concentrations in the submaxillary gland, vas deferens⁶⁾ and liver are much lower than previous

Table 5. Adrenaline and noradrenaline contents of some organs of rats in basal conditions

Organs or tissues	Adrenaline (nmol/g)	Noradrenaline (nmol/g)	Adrenaline (%)	References
Heart	0.240	4.26	6 ^{a)}	Goodall (1951) (17)
	0.117	3.83	3	Hököfelt (1951) (8)
	0.273	3.25	8	Strömblad & Nickerson (1961) (16)
	0.437	7.39	6	Moore & Brody (1961) (12)
	0.273	1.59	17	Anton & Sayre (1962) (5)
	0.055	4.63	1.2	Pendleton et al. (1978) (18)
	0.073	—	—	Kvetnansky et al. (1979) (3)
	0.20	6.51	3	Fredholm et al. (1979) (9)
	0.055	4.42	1.2	Present results
	0.382	2.78	14	Anton & Sayre (1962) (5)
Spleen	0.034	6.16	0.6	Present results
Submaxillary gland	0.60	7.27	8	Strömblad & Nickerson (1961) (16)
	0.25	5.62	4	Euler & Ryd (1963) (15)
	0.0082	8.02	0.1	Sudo (1985) (6)
	0.39	32.8	1.2	Kvetnansky et al. (1979) (3)
Vas deferens	0.023	70.8	0.03	Sudo (1985) (6)

^{a)} : Adrenaline/(Adrenaline + Noradrenaline) (%)

results.^{3,8,15)} This discrepancy could be attributed partially to differences in specificity and sensitivity of the methods used to measure adrenaline.

Plasma levels of catecholamines seem to be affected by the conditions of blood sampling.^{19,20)} According to Popper *et al.*¹⁹⁾ adrenaline concentration in plasma obtained from the trunk of the body after decapitation is above 45 pmol/ml, while that obtained through indwelling catheters is about 1 pmol/ml in resting rats. In the present experiment, blood was collected under urethane-chloralose or pentobarbital anaesthesia and the plasma level of adrenaline in control rats was slightly higher than in catetherized rats.^{19,20)} The present data, however, clearly showed that swimming for four hours caused a marked increase in the plasma level of adrenaline. The rate of the swimming-induced increase in plasma adrenaline was not as pronounced as that in urinary adrenaline. This might be due to the higher level of plasma adrenaline observed in the control group, as described above.

Since exogenously administered adrenaline is taken up in various organs of animals,^{16,21-24)} it was expected that adrenaline released from the adrenal medulla would accumulate in the organs during exposure to stressful situations. More than three decades ago, Hökfelt⁸⁾ found that swimming produces an increase in adrenaline contents of the rat heart and liver. Our previous observations⁶⁾ confirmed this finding and further indicated that swimming induces an increase in adrenaline content in other extra-adrenal peripheral organs such as the kidney, vas deferens, abdominal wall muscle, submaxillary gland and spleen. Hökfelt measured adrenaline levels in the heart and liver after 30-, 60- and 90-min periods of swimming, but the results did not show a clear relationship between the increase of adrenaline in the organs and the duration of swimming.⁸⁾ The present results definitely indicated a time-dependent increase in adrenaline content of the organs during the stress of swimming. A time-dependent decrease in the adrenal content of adrenaline and a marked increase in plasma level and urinary excretion of adrenaline were also found. These observations support the hypothesis that adrenaline is released from the adrenal medulla to the circulation under stressful conditions, and that circulating adrenaline is taken up in various peripheral organs, resulting in an increase in adrenaline concentration of the organs.

It has been reported that heart rate shows a time-related increase during strenuous physical exercise in man. Ekelund and Holmgren²⁵⁾ found continuously increasing heart rate and falling systemic arterial blood pressure in 60-min periods of physical exercise. Furuya and Kubota²⁶⁾ also described a gradual increase in heart rate during exercise on a bicycle ergometer in untrained college students. These patterns of change in heart rate are similar to those in adrenaline content of the heart observed in the present study.

Brown and Macquin²⁷⁾ measured pulse rate and plasma adrenaline level in healthy volunteers after adrenaline infusion. They found that pulse rate remained elevated for several hours despite a rapid fall in plasma adrenaline concentration

and that this increase in pulse rate was abolished or reduced by pretreatment with desmethyylimipramine, a neuronal uptake inhibitor. As shown by Anden²¹⁾ and Iversen,²³⁾ some of the labelled adrenaline taken up in mammalian organs is retained for several hours after adrenaline injection. The present results indicated that adrenaline level in the organs was still considerably high compared with the control three hours after the cessation of a 4-hour period of swimming. These observations suggest that organ adrenaline, perhaps localized in nor-adrenergic nerve endings, plays a physiological role in circulatory responses to stressful exercise.

In many stressful situations, however, heart rate often shows a rapid increase in the early stages.²⁸⁾ The present results indicated no significant increase in adrenaline content of the heart after 20 minutes of swimming. The initial responses of heart rate to stressful conditions may be associated with different mechanisms from those in which adrenaline in the heart is assumed to be involved.

Circulating adrenaline does not enter the central nervous system because of the blood-brain barrier.²²⁾ In the present study, changes in central adrenaline concentrations were quite different from those in peripheral adrenaline concentrations during swimming, that is, adrenaline concentration decreased in the brain regions time-dependently, while it increased in peripheral organs. The pons-medulla showed a significant increase in adrenaline content 24 hours after swimming, but none of the peripheral organs indicated such a change. Since central adrenaline is mainly synthesized in adrenaline neurons in the pons-medulla, the increase of adrenaline in this region might be associated with enhanced activity of the adrenaline-forming enzyme PNMT after stress exposure.¹⁴⁾ It is assumed that the physiological role of central adrenaline in adapting to stressful conditions might be different from that of peripheral adrenaline.

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