as continuous jumping and running while in their cages. Finally, we observed that the zinc deficient animals showed a mean final body weight of 31.8 ± 0.9 compared to 41.4 ± 1.0 g for control animals. This is in agreement with investigators who have found zinc deficiency to result in growth cessation and weight loss[12,13].

Whereas no hypothesis has been previously suggested for the increased activity level in zinc deficiency, it is well established that zinc participates in at least 18 metalloenzyme[14] systems and is essential for normal protein synthesis through its direct effect on deoxyribonucleic acid polymerase[15]. It seems likely that in a state of zinc deficiency, various biochemical pathways may be disrupted resulting in decreased production of metabolites such as CNS neurotransmitters whose function is primarily in primarily inhibitory. Future studies might measure the concentration of these neurotransmitters in zinc deficient CNS tissue and compare these levels to those found in control animals.

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Thermogenic response as the function of extravascular influx of infused noradrenaline

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Summary. The dynamic and static phases of the thermogenic response to i.v. infused noradrenaline (NA) do not reflect the arterial concentration of NA; according to the equation presented here they are a function of the influx rate.

Thermogenesis of cold-acclimatized rats in the cold is accompanied by enhanced arterial concentration of noradrenaline (NA)[1,2]. Furthermore, injection[3] or infusion[4] of NA evokes a thermogenic response in the same animals placed in the thermoneutral zone. In spite of the fact that thermogenesis is stimulated by NA, the magnitude of the thermogenic response is not controlled by the arterial concentration of NA[5]. In the present report we have derived an equation, describing (under the 2 generally-accepted assumptions that: A) the thermogenic response is a classical function of inner-receptor-concentration of NA; B) the receptor acting NA is removed enzymatically) the inner concentration of NA as the function of extravasal influx of i.v. infused NA. We thus obtained an approximation of experimental thermogenic values.

Material and methods. Male Sprague-Dawley albino rats were acclimatized to cold by a standard procedure. Before each experiment in a barbital-sedated rat of 341 g average weight the external jugular vein was cannulated for infusion of NA. The aorta was catheterized via the carotid artery for measuring arterial concentration of NA and blood pressure. Plasma concentration of NA was measured radioenzymatically[6]; blood pressure by the direct route, using a transducer. Total thermogenesis was measured as the oxygen consumption by an open circuit method, using a paramagnetic oxygen analyser.

Results. Changes in the functional inner NA concentration (c) are given by the difference between influx (i) and efflux (e) NA rate into and from inner space:

$$V\dot{c} + e = i \qquad (1)$$

where V = constant volume of the inner space

$$c = c_{min}\Delta c$$
$$e = e_{min}\Delta e$$
$$i = i_{min}\Delta i$$

It follows from the condition of initial steady-state that:

$$e_{min} = i_{min}$$

Then

$$V\Delta\dot{c} + \Delta e = \Delta i \qquad (2)$$

For transformation to the relative form, the following variables are defined:

$$c_r = \Delta c/K;\ e_r = \Delta e/\Delta e_{max};\ i_r = \Delta i/\Delta e_{max}$$

where K is a constant with the size of concentration.

Quasi-stationary values of 4 variables during different infusion rates of noradrenaline (NA)

Infusion rate ($ng\ NA \cdot g^{-1} \cdot min^{-1}$)	0	0.4	1.0	2.0	4.0	6.0
Metabolic response ($ml\ O_2 \cdot g^{-1} \cdot h^{-1}$)	0	0.23	0.81	1.48	2.01	2.21
m_r*	0	0.102	0.353	0.643	0.875	0.960
Plasma concentration ($ng\ NA \cdot ml^{-1}$)	0.46	1.70	2.88	7.68	10.90	19.44
Δc_p	0	1.24	2.42	7.22	10.44	18.98
Blood pressure (kPa)	15.26	15.53	16.10	17.29	21.68	21.68
Δp	0	0.27	0.84	2.03	6.42	6.42
Digressed influx ($\Delta i = \Delta p \cdot \Delta c_p$)	0	0.33	2.03	14.65	67.02	121.85

Each value is the mean from 3 experiments. * $m_r = 1$ for maximal metabolic response 2.3 $ml \cdot g^{-1} \cdot h^{-1}$.

Using the relationship of the assumption B for e_r:

$$e_r = \frac{1}{\frac{K}{\Delta c} + 1} = \frac{1}{\frac{1}{c_r} + 1}$$

and substituting into equation (2), we obtain:

$$V K \dot{c}_r + \Delta e_{max} \frac{1}{\frac{1}{c_r} + 1} = \Delta e_{max} i_r$$

yielding

$$a(1 + c_r)\dot{c}_r + (1 - i_r)c_r = i_r \qquad (3)$$

where a is a constant ($a = VK/\Delta e_{max}$)

The influx rate is considered as a product of arterial NA concentration and transcapillary flow rate. The transcapillary exchange with laminar blood flow is described by Henry-Poiseuille's law, according to which the flow is proportional to the pressure gradient. The pressure gradient is approximated in the table by arterial blood pressure.

For the evaluation of i_r the constant Δe_{max} is experimentally unknown and has to be calculated in the following manner. It follows from the steady-state equation (3) for c_r that $c_r = i_r/(1 - i_r)$. The substitution by the definition relationship for i_r yields:

$$c_r = \Delta i/(\Delta e_{max} - \Delta i) \qquad (4)$$

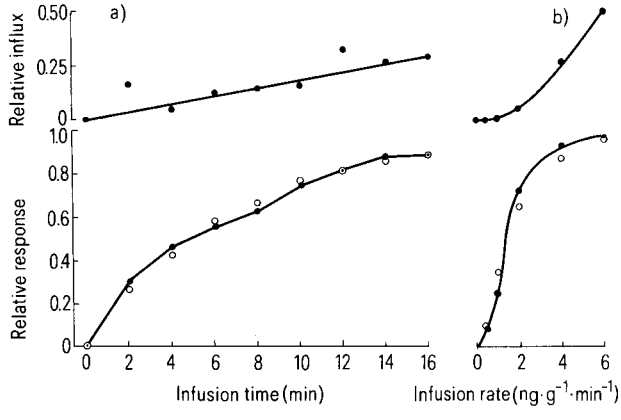
Another expression for c_r can be derived from the relationship for the response (m_r) of the assumption A: $m_r = 1/(K_m/\Delta c) + 1$ and from the definition of c_r:

$$c_r = \frac{K_1 \cdot m_r}{1 - m_r} \qquad (5)$$

Putting terms 4 and 5 into the equation and using experimental data Δi and m_r for different infusion rates, we obtain a set of equations for 2 unknown constants K_1 and Δe_{max}, from which an average value of both constants can be calculated.

The relative influx and metabolic response calculated in this manner are presented in the figure, B. According to equation (3), the influx and the response were also calculated with respect to the infusion time, using an analogue computer (fig. A). The figure shows that dynamic and static phases of the metabolic response are well approximated by the calculated data.

Discussion. The fact that the thermogenic response to infused NA is not proportional to arterial concentration of NA[5] appears to agree with the finding that warm-acclimatized rats have a higher arterial concentration of NA although their NA thermogenesis is negligible, in comparison with cold-acclimatized rats, which are characterized by a large thermogenic response[7]. The necessity of multiplying the arterial concentration by transcapillary flow rate (approximated in this work by arterial pressure) is in accordance with both conclusions[5,7]. This fits in well with the experimental results and suggests that the flow (resulting from influx and efflux rate of NA into- and from the functional inner space) is a complementary part of the adrenergic control of thermogenesis.



A Relative influx, calculated (●) and measured (○) relative metabolic response from the start of NA infusion at the rate 6 ng $NA \cdot g^{-1} \cdot min^{-1}$. *B* The same 3 parameters during quasi-stationary state of metabolic response to different infusion rates of NA. Each value is the mean from 3 experiments. For the manner of calculation see text.

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