tially, or that the enzyme found in the joint has a local source. It would be interesting to see if some other smaller adrenergic vesicular proteins, such as chromogranins which have a mol. wt of 70,000, and are also released along with NA during sympathetic nerve stimulation[2], are present in higher amounts than DBH in synovial fluid. This would clarify the source of the DBH present in synovial fluid. Little is known about the sympathetic innervation of the joint, but it may be that the enzyme comes from sympathetic nerves innervating the joint structures, such as the synovial membrane whose cells have secretory functions. These nerves might regulate the secretory functions of these cells, or other functions of the joints, such as the amount and composition of synovial fluid, a critical factor for the adequate lubrication of the joint cartilage.

Increased cardiac noradrenaline turnover in the rat after acute exposure to environmental heat

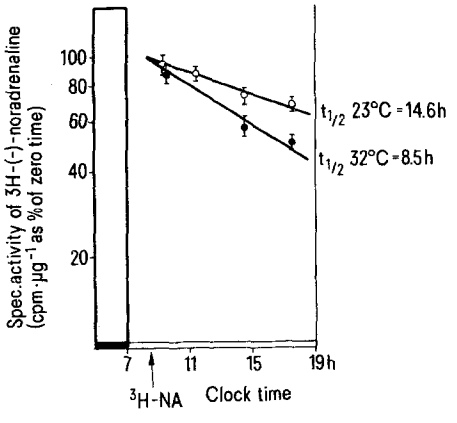
R. Saller and B. Lemmer[1]

Zentrum der Pharmakologie, Theodor-Stern-Kai 7, D-6000 Frankfurt am Main (Federal Republic of Germany, BRD), 5 November 1976

Summary. In male rats, the cardiac turnover of noradrenaline is significantly increased on acute exposure to an environmental temperature of 32 °C, when compared to control experiments performed at 23 °C.

Various environmental factors influence the metabolism and the turnover of noradrenaline in the rat heart, e.g. grouping of the animals[2], state of training[3], light and darkness[4], high altitude influence[5] and various factors which are stressing the animals[6]. Furthermore, acute and long-term exposure to cold increase the cardiac noradrenaline turnover in rats[7], and environmental heat increases the noradrenaline turnover in the hypothalamus[3], which plays an important role in the thermoregulation in the rat[8], and in other areas of the rat brain[9]. As the cardiac output and the heart rate was reported to be increased at an elevated room temperature[10], it was the aim of this study to investigate whether these changes may in turn be due to an increased turnover rate of the physiological transmitter substance, noradrenaline, in the rat heart.

Materials and methods. In the experiments, male Wistar rats (TNO W.70) of about 130–160 g were used. The animals were kept for at least 5 days under a controlled lighting schedule of 12 h light (7.00–19.00 h) alternating with 12 h darkness (19.00–7.00 h) with food and water ad libitum and at a room temperature of 23 ± 1 °C. The noradrenaline turnover in the hearts was determined in the period of light from the logarithmic decline of the specific activity after i.v. injection of 10 μCi/kg 3H-(–)-noradrenaline (Radiochemical Centre, Amersham, spec. activity 8.7 Ci/mmole) as described in detail previously[4]. The noradrenaline concentration was determined according to Chang[11]. Heat experiments were performed at a room temperature of 32 ± 1 °C, and in order to achieve this temperature the usual environment of the animals was heated up from 7.00 h until the beginning of the experiment at 8.30 h. Control experiments were performed in the same week at a normal room temperature of 23 ± 1 °C. Significance was tested by the unpaired 2-tailed Student's t-test, and linearity of the regression functions was proved by the F-distribution.



Decay of the specific activity of noradrenaline in the rat heart after i.v. injection of 10 μCi/kg 3 H-(–)-noradrenaline in the period of light at a room temperature of 23 °C (○—○) or 32 °C (●—●). Arrow indicates time of injection at 8.30 h (zero time). Each point represents the mean value ± SEM from 5 animals.

Results. The endogenous noradrenaline concentration in the hearts was increased by the acute exposure to heat from 0.94 ± 0.02 $\mu g \times g^{-1}$ (n = 43) at a normal temperature to 1.04 ± 0.02 $\mu g \times g^{-1}$ (n = 43). This increase was statistically significant ($p < 0.001$). In the figure, one representative experiment out of each experimental group is depicted, showing that the half-life of the specific activity of the cardiac noradrenaline is decreased when the environmental temperature is increased from 23 °C to 32 °C. All experimental results are summarized in the table. It can be seen that acute exposure to an elevated room temperature of 32 °C during light significantly increased the turnover rate of noradrenaline in the rat heart (0.069 $\mu g \times g^{-1} \times h^{-1}$) when compared with the control experiments performed at a room temperature of 23 °C (0.039 $\mu g \times g^{-1} \times h^{-1}$). Thus, the mean half-life was decreased to 10.2 h at 32 °C from 16.3 h at 23 °C.

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Turnover of noradrenaline in rat heart during the period of light at a room temperature of 23 ± 1 °C and 32 ± 1 °C resp.

Room temperature: 23 ± 1 °C			Room temperature: 32 ± 1 °C		
Half-life $t_{1/2}$ (h)	Rate constant k (h^{-1})	Turnover rate ($\mu g \times g^{-1} \times h^{-1}$)	Half-life $t_{1/2}$ (h)	Rate constant k (h^{-1})	Turnover rate ($\mu g \times g^{-1} \times h^{-1}$)
17.7	0.0392	0.035	11.0	0.0629	0.057
14.6	0.0475	0.045	11.7	0.0594	0.063
17.8	0.0389	0.038	8.5	0.0818	0.074
15.7	0.0442	0.040	10.3	0.0675	0.081
$\bar{X}$ 16.3(14.1–19.4)*	0.0425	0.039	10.2(8.3–13.3)*	0.0679**	0.069**
SEM	± 0.0020	± 0.002		± 0.0049	± 0.006

The parameters of the turnover were calculated from decay of the specific activity after i.v. injection of ^{3}H-(–)-noradrenaline. Mean values ± SEM of 4 separate experiments at either room temperature. *Geometric mean with 95% confidence limits. **p (control to heat) < 0.005.

Discussion. Until now no data are available demonstrating the effect of an elevated environmental temperature on the cardiac turnover of noradrenaline in the rat. The experimental results presented here clearly show that an acute increase in environmental temperature from 23°C to 32°C results in a significantly increased cardiac turnover of noradrenaline in the rat. Such an elevation in the room temperature leads to an increase in the rectal temperature[9], to an increased sympathetic nervous activity in some peripheral organs[12] and to an increase in the cardiac output mainly due to an elevated heart rate[10]. Thus, the increased cardiac turnover of noradrenaline on acute exposure to heat can be explained as a consequence of an accelerated sympathetic nervous activity. However, it remains unsolved whether the increased turnover is due to a specific effect of heat on the thermoregulatory centers[8], thereby increasing the peripheral sympathetic nervous system, or whether a non-specific stress reaction takes place[8].

The results presented here together with earlier findings demonstrating circadian variations in the cardiac turnover of noradrenaline[4] and the dopamine turnover in rat brain[13], further indicate the importance of exact standardization of experimental conditions in animal studies. The importance of a controlled thermal environment was already shown by Fuhrman and Fuhrman[14] and Weihe[15] who could demonstrate that variations in environmental temperature greatly influence the sensitivity of experimental animals to drugs, leading to variations of results in drug testing.

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Fluorescence histochemical demonstration of the uptake of dopamine-derived dihydroisoquinoline in the hypothalamic neurons

S. Partanen

Department of Biomedical Sciences, University of Tampere, Box 607, SF-33101 Tampere 10 (Finland),
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Summary. The uptake and the accumulation of dopamine-derived fluorescent dihydroisoquinoline were demonstrated with direct fluorescence histochemistry in the hypothalamic dopaminergic neurons, in the nerves of the neurointermediate lobe, and in some endocrine cells of the hypophysis of the rat.

It has been suggested that the in vivo formation of tetrahydroisoquinolines (TIQs) derived from the condensation of catecholamines (dopamine, noradrenaline and adrenaline) with aldehydes produced in the metabolism of alcohols plays a part in the pathological manifestation of alcohol intoxication and dependence[1–3]. Furthermore, an increase in dopamine concentration in the tissues might lead to the formation of dopamine-derived TIQs produced in the condensation reaction between dopamine and acetaldehyde or 3,4-dihydroxyphenylacetaldehyde[4,5]. Another possible route to the formation of biologically active isoquinolines and β-carbolines is the enzymatic production of formaldehyde from 5-methyltetrahydrofolic acid and subsequent condensation of the formaldehyde with catecholamines or indolamines[6,7]. TIQs are taken up by an active, desmethylimipramine- and cocaine-sensitive mechanism in the nerve endings, and released upon stimulation of the nerves, giving rise to the postsynaptic effect[1].

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