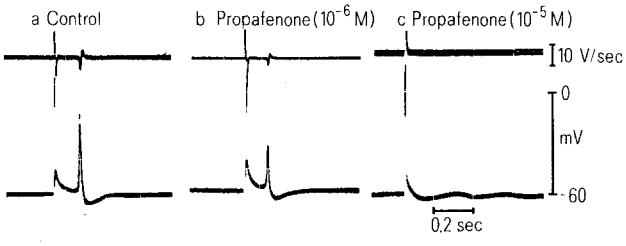
face of the vessel. The arterial segments were placed in a non-recirculating organ bath and suffused with a physiological salt solution (PSS) containing (in mM): Na^+, 141; K^+, 4.7; Ca^{++}, 2.5; Mg^{++}, 0.76; Cl^-, 124; $H_2PO_4^-$, 1.7; HCO_3^-, 25; and glucose, 11. The solutions were aerated with 95% oxygen – 5% carbon dioxide (pH 7.3–7.4) and maintained at 37 °C. Tetraethylammonium chloride (10 mM) was added to induce excitability. Propafenone - HCl (Knoll AG, Ludwigshafen, Batch No. W33425) was added to the bathing solution at final concentrations of 10^{-6}–10^{-5} M. Transmembrane and action potentials were recorded with glass microelectrodes as previously described[6].

Results and discussion. The effect of propafenone on the resting membrane potential (E_m), amplitude and maximal rate of rise ($+\dot{V}_{max}$) of the TEA-induced action potential are summarized in the table. Addition of propafenone to the bathing solution caused a dose-dependent reduction in both amplitude and $+V_{max}$ of the action potential (figure). High doses (10^{-5} M) of propafenone also resulted in a small but significant reduction in E_m (table).

Since it has been shown that the TEA-induced action potential in canine coronary VSM is dependent upon extracellular Ca^{++} and are blocked by Ca^{++} antagonists, it is reasonable to conclude that the underlying inward current mediating these action potentials is carried by Ca^{++}[6,7]. The findings that propafenone markedly inhibits both the amplitude and rate of rise of the TEA-induced action potential suggests that one of its mechanisms of action is to inhibit Ca^{++} inward current in coronary VSM. Such a hypothesis is supported by the findings that propafenone reduces Ca^{++} inward current in cardiac muscle[8].



Effect of propafenone on the amplitude and maximal rate of rise ($+\dot{V}_{max}$) of the TEA-induced Ca^{++} dependent action potential in vascular smooth muscle of canine coronary arteries. *A* Control action potential induced by extracellular stimulation in the presence of 10 mM TEA. *B* Record from same cell showing a marked reduction in both the amplitude and $+\dot{V}_{max}$ of the TEA induced action potential by 10^{-6} M propafenone. *C* Complete inhibition of the action potential upon raising the concentration of propafenone to 10^{-5} M. Voltage, time and $+\dot{V}_{max}$ calibrations in C apply throughout.

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Diurnal variations in thermoregulatory responses to intrahypothalamic and intravenous injections of noradrenaline in the pigeon

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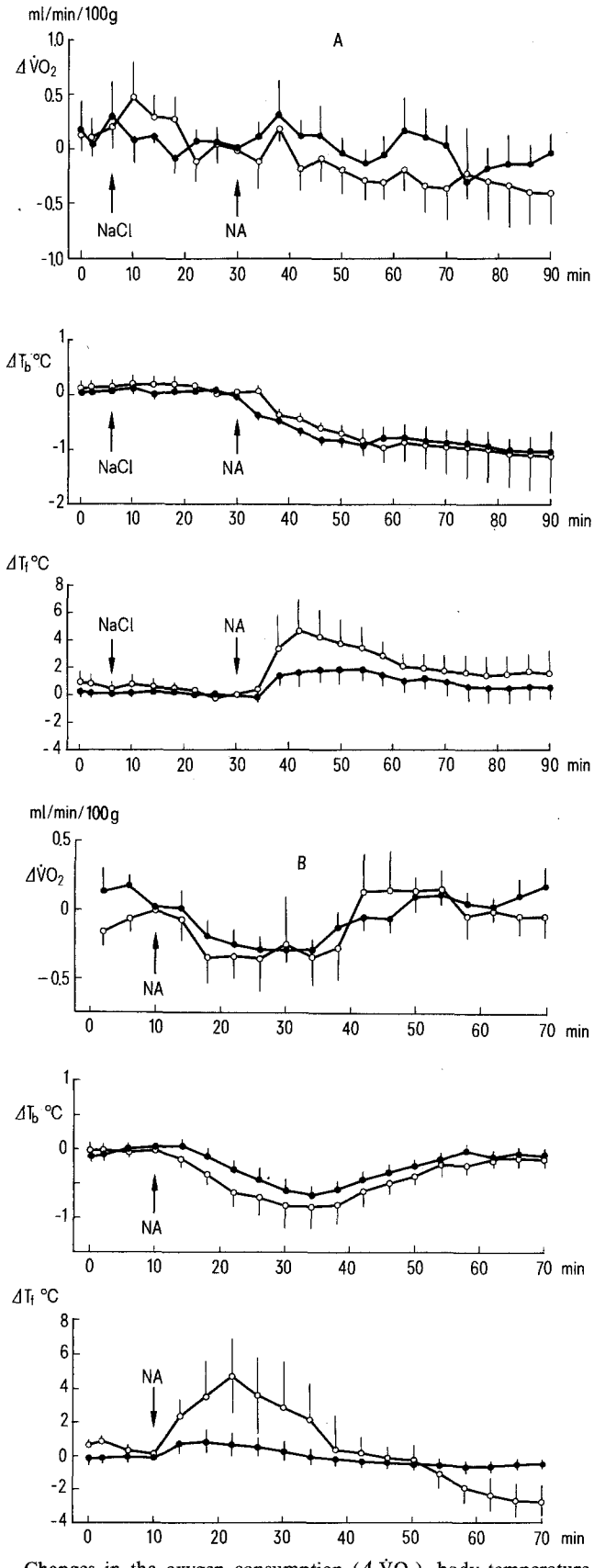
Summary. The differences in responses of T_b, T_f and $\dot{V}O_2$ both to intrahypothalamic and i.v. administration of NA were measured both at noon and at midnight in the pigeon. Although the T_b and $\dot{V}O_2$ were at a higher level in the daytime, no differences in the magnitude of the fall in $\dot{V}O_2$ and T_b were obtained after either intrahypothalamic or i.v. injections of NA, whether it was measured during the day or at night. The only marked difference was the more prominent vasodilatation in the daytime after both routes of injection.

It is generally accepted that both the basal metabolic rate (BMR) and body temperature (T_b) show a diurnal variation in birds[1,2]. The pigeon, a typical day-active bird, displays its lowest T_b and $\dot{V}O_2$ at night[3]. It has been shown that both peripheral and intracerebral applications of noradrenaline (NA), in contrast to the results obtained in mammals, result in hypothermia[4,5]. This is at least partly associated with the impairment of shivering and increased heat loss resulting from the induced vasodilatation in the foot. Petrović et al.[6] have demonstrated a clear diurnal rhythm in the thermogenic response to NA in rats, which seems to be related to the accompanying changes in thyroid gland activity.

To test whether the degree of hypothermia after either peripheral or intrahypothalamic injections of NA is related to the endogenous diurnal changes in physiological activities in the pigeon, the injections were conducted both at 12.00 h and at 24.00 h.

Materials and methods. Experiments were performed with 11 adult Pigeons, weighing 290–370 g, at the environmental temperature of + 15 °C. Birds were divided into 2 groups. Group 1 was i.v. injected (tibial vein) with NA (1-arterenol bitartrate, Sigma, 0.4 mg/kg in 0.85% NaCl-solution). Group 2 was injected intrahypothalamically (PO/AH-area) with 10 µg NA per 1 µl. For intrahypothalamic injections a guide cannula was unilaterally implanted as described earlier[7,8]. The coordinates were 7.8–8.0 mm anterior from the intra-aural line and 1.0–1.5 mm lateral from the midline and 8.6–10.0 mm below the surface of calvarium. The details for measuring $\dot{V}O_2$ are given elsewhere[9]. In control experiments performed with the same animals an equal volume of NaCl-solution was given. The injections were made in the daytime at 12.00 h in a lighted environmental chamber and at night at 24.00 h in a darkened chamber.



Changes in the oxygen consumption ($\Delta \dot{V}O_2$), body temperature (ΔT_b) and foot temperature (ΔT_f) of the pigeons after intravenous (A) and intrahypothalamic (B) injection of noradrenaline (NA) at +15 °C at 12.00 h (○——○) and at 24.00 h (●——●). Each point represents the mean ± SE of 6 (A) or 5 (B) pigeons.

Results and discussion. Mean $\dot{V}O_2$, T_b and foot temperature (T_f) before injections were; 2.8±0.15 ml · (min · 100 g)$^{-1}$ ($\bar{X}$±SEM, n=11), 41.9±0.19 °C and 20.8±0.77 °C at 12.00 h and 2.4±0.12 ml · (min · 100 g)$^{-1}$, 40.8±0.23 °C and 19.7±1.0 °C at 24.00 h, respectively. Statistically significant differences were observed between the day and night values of T_b($p < 0.001$, one-way t-test) and $\dot{V}O_2$ ($p < 0.05$). No significant differences were seen in the degree of fall in $\dot{V}O_2$ and T_b after either i.v. or intrahypothalamic injections of NA at noon or at midnight (figure, A and B). The only marked difference was seen in the vasodilatatory effect of NA observed after injection by both routes. In intrahypothalamic injections the mean maximal increase in T_f was 4.6±2.2 °C (n=5, $p < 0.05$) at 12.00 h but at 24.00 h only 0.9±0.7 °C (not significant=NS) when compared to the preinjection level. Parallel results were obtained with the i.v. injections of NA: 4.7±2.3 °C (NS) and 2.0±1.0 °C (NS), respectively. Saline injections were without any significant effects on the parameters measured.

Since both $\dot{V}O_2$ and T_b were statistically at a higher level at day than at night the decreased values of these parameters were also at a higher level at noon than at midnight after injections. If we suppose that NA eliminates heat production in the pigeon only by impairing shivering, as shown in our earlier experiments[4,5], and its abolition is quantitatively similar both during the day and at night, then the differences in $\dot{V}O_2$ after injections represent only diurnal variations in BMR.

The different responses to NA in T_f at noon and at midnight might result in changes in the peripheral vasoconstriction as a consequence of the supposed differences in the arousal state of the pigeons during the day and night measurements. The similar response observed in T_f both after i.v. and after intrahypothalamic injections might be explained by the central effects of i.v. NA. That peripherally applied NA may affect the hypothalamic thermoregulatory area has previously been shown by Hissa and Pyörnilä[10]. The peripheral vasomotoric effects of NA are not, however, excluded; Nolan et al.[11] have provided evidence of beta-adrenergic stimulation resulting in vasodilatation of the wattle in chickens. The presumed sites of the thermoregulatory actions of NA in birds has recently been discussed more widely by Hissa et al.[9].

In conclusion, these experiments provide data which show that the magnitude of the fall in $\dot{V}O_2$ and T_b produced by either intrahypothalamic or i.v. administrations of NA is independent of the diurnal variations of BMR and T_b.

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