Eur J Appl Physiol (1989) 58:879–883

European Journal of Applied Physiology and Occupational Physiology

Plasma norepinephrine and heart rate dynamics during recovery from submaximal exercise in man

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Summary. The time course of heart rate (HR) and venous blood norepinephrine concentration [NE], as an expression of the sympathetic nervous activity (SNA), was studied in six sedentary young men during recovery from three periods of cycle ergometer exercise at 21%±2.8%, 43%±2.1% and 65%±2.3% of $\dot{V}_{O_{2max}}$ respectively (mean±SE). The HR decreased mono-exponentially with τ values of 13.6±1.6 s, 32.7±5.6 s and 55.8±8.1 s respectively in the three periods of exercise. At the low exercise level no change in [NE] was found. At medium and high exercise intensity: (a) [NE] increased significantly at the 5th min of exercise (Δ[NE]=207.7±22.5 pg·ml^{-1} and 521.3±58.3 pg·ml^{-1} respectively); (b) after a time lag of 1 min [NE] decreased exponentially (τ=87 s and 101 s respectively); (c) in the 1st min HR decreased about 35 beats·min^{-1}; (d) from the 2nd to 5th min of recovery HR and [NE] were linearly related (100 pg·ml^{-1} Δ[NE]≃5 beats·min^{-1}). In the 1st min of recovery, independent of the exercise intensity, the adjustment of HR appears to have been due mainly to the prompt restoration of vagal tone. The further decrease in HR toward the resting value could then be attributed to the return of SNA to the pre-exercise level.

Key words: Heart rate — Norepinephrine — Recovery — Exertion

Introduction

In a previous paper (Orizio et al. 1988) the relationship between the time course of heart rate (HR) and venous blood norepinephrine concentration [NE], a blunt expression of sympathetic system activity (Christensen and Galbo 1983; Wallin et al. 1987), has been analysed in the transition phase from rest to submaximal exercise. Experimental evidence showed that the increases in HR and [NE] are significantly related only at exercise intensities higher than about 30% of the maximal oxygen consumption ($\dot{V}_{O_{2max}}$). Moreover, the mathematical description of HR changes enabled the evaluation of the relative roles of the sympathetic and parasympathetic drives in the control of HR during the on-phase of a dynamic task.

On stopping exercise of submaximal intensity, the HR decreases immediately and returns to its resting value. The return of the HR follows an exponential kinetic (Davies et al. 1972; Hagberg et al. 1980) which can be described by a second order exponential function when the exercise intensity is higher than 40% $\dot{V}_{O_{2max}}$ (Broman and Wigertz 1971; Linnarson 1974).

The changes of [NE] during recovery have already been investigated, but only at high exercise intensities and an exponential decrease, with $t_{\frac{1}{2}}$ values between 2 to 10 min, has been observed (Hagberg et al. 1979; Watson et al. 1980).

As far as we know, no study has yet defined the changes in [NE] with frequent blood sampling during the first minutes of recovery. Thus, in order to gain some insights into the relative roles of the sympathetic and parasympathetic systems in the control of the cardiac frequency during recovery, the inter-relationship between HR and [NE] has been studied.

Materials and methods

The characteristics of the subjects and the experimental procedure are described in detail in a companion paper (Orizio et

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al. 1988). Therefore, only the information relevant to the present study will be given here.

Six healthy sedentary males (age: 23.5±0.9 years, mean±SE; $\dot{V}_{O_2max}$: 44.8±1.5 ml·kg^{-1}·min^{-1}) volunteered to participate in the study (for details see Table 1 in Orizio et al. 1988; subject DF is not included in the present investigation).

The exercise consisted in pedalling for 5 min at 50 rpm on a Monark cyclo-ergometer Sweden, Ergomedic 818-E at constant loads (50, 100 and 150 W; low-, medium- and high-exercise intensity respectively), in a randomized sequence, with a 3-day interval between consecutive tests.

The electrocardiographic signal was monitored continuously and fed on-line into a computer (IBM AT U.S.A.) during rest, exercise and a 5-min recovery period. An off-line beat-by-beat analysis was carried out in order to define the time course of HR during the transition from exercise to rest. The transient responses of HR were subjected to dynamic analysis by adopting the following mono-exponential and bi-exponential functions, respectively:

$$HR_{(t)} = a_0 + b_1 \cdot e^{-t/\tau_1} \quad (1)$$

$$HR_{(t)} = a_0 + b_1 \cdot e^{-t/\tau_1} + b_2 \cdot e^{-t/\tau_2} \quad (2)$$

where a_0 is the asymptotic value of HR, b_1 is the decrement below the HR value at the end of the exercise for $t = \infty$ and τ is the time constant. In Eq. 2, b_1 and b_2 indicate the HR decrement described by the two components of the function, whose time constants are τ_1 and τ_2, respectively ($\tau_1 < \tau_2$). When stepwise regression analysis (Kendall et al. 1983) showed that the contribution of b_2 (i.e. the contribution of the slow component of the bi-exponential function) did not pass the tolerance test, having a tolerance value of 0.01 (Dixon 1983), the kinetic of HR was then described by the mono-exponential function.

Plasma [NE] was determined by means of high-pressure liquid chromatography (Goldstein et al. 1981; Beschi et al. 1987). With the subject on the cycle, the blood samples were collected via an antecubital venous catheter at rest, after 5 min of exercise and after 20, 50, 90, 140, 190 and 300 s of recovery.

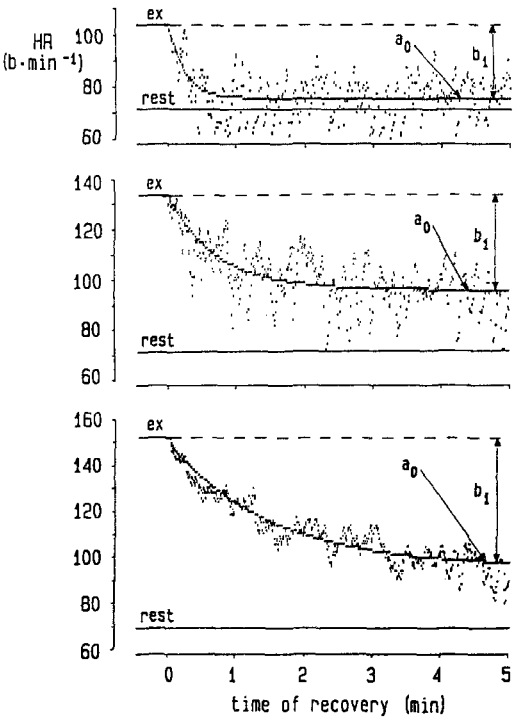

Fig. 1. Beat-by-beat heart rate (*HR*) values during the recovery from low- (50 W), medium- (100 W) and high- (150 W) exercise intensities are shown for a representative subject (PE), together with the best fit *exponential curves*. The parameters of the mathematical functions are reported in Table 1

Results

The oxygen demand at 50, 100 and 150 W corresponded to 21.5%±2.8% $\dot{V}_{O_2max}$ (range 15%–33%), 43.3%±2.1% $\dot{V}_{O_2max}$ (range 38%–51%) and 64.8%±2.4% $\dot{V}_{O_2max}$ (range 55%–70%), respectively. All results are given as mean±SE.

Heart rate. Mean resting HR values were 71.0±4.6 beats·min^{-1}, 68.3±4.5 beats·min^{-1} and 70.3±2.6 beats·min^{-1} prior to the three exercise periods respectively. At the 5th min of exer-

Table 1. Parameters of best fit function of heart rate (HR) changes in the recovery from exercise according to Eq. 1

	Low exercise						Medium exercise						High exercise					
Subject	HR rest	HR end of exercise	a_0	b_1	τ_1	ε	HR rest	HR end of exercise	a_0	b_1	τ_1	ε	HR rest	HR end of exercise	a_0	b_1	τ_1	ε
BT	87	107	85	−22	13.3	6.2	73	112	87	−25	37.8	6.0	76	138	97	−41	48.9	5.9
CD	65	84	70	−14	14.4	7.8	57	117	61	−56	43.3	8.2	64	135	75	−60	38.9	8.9
PE	72	104	75	−29	13.3	8.2	71	134	96	−38	42.4	9.2	74	153	102	−51	85.9	4.7
RF	81	102	74	−28	12.4	6.8	86	142	97	−45	41.6	9.7	75	155	95	−60	49.9	8.1
SE	63	84	61	−23	8.0	8.9	66	122	86	−36	9.9	9.5	72	148	91	−57	74.5	5.7
VL	58	94	63	−31	20.0	5.2	57	121	70	−51	21.4	5.4	61	150	85	−65	37.0	6.3
Mean ±SE	71.0 ±4.6	95.8 ±4.1	71.3 ±3.6	−24.5 ± 2.5	13.56 ±1.58		68.3 ±4.5	124.7 ±4.6	82.8 ±5.9	−41.8 ± 4.6	32.73 ±5.65		70.3 ±2.6	146.5 ±3.3	90.8 ±3.9	−55.7 ± 3.5	55.85 ±8.12	

Individual and mean values of HR (beats·min^{-1}) at rest and at the end of exercise; a_0 (beats·min^{-1}) asymptotic value of HR; b_1 (beats·min^{-1}) decrement of HR below the exercise value for $t = \infty$; τ (s) time constant of exponential curve. ε is the residual between the experimental and computed values

cise the corresponding increase in HR (Δ HR) was 24.8 ± 2.9 beats·min^{-1}, 56.3 ± 3.7 beats·min^{-1} and 76.2 ± 3.7 beats·min^{-1}, respectively.

At the end of each exercise the HR decreased immediately. The best fit function was always found to be mono-exponential, independent of the subject and work intensity. In Fig. 1, the beat-by-beat HR values observed during recovery at each exercise level are shown for a representative subject (subject PE), together with the best fit exponential curves.

The individual and mean values of the parameters of Eq. 1 are listed in Table 1 together with the corresponding pre-exercise HR value and the HR value at the end of the exercise. Variance analysis showed that τ values increase significantly with exercise intensity.

In Fig. 2A the mean HR values observed when blood samples were collected are shown during the first 5 min of recovery. HR had already reached the pre-exercise value 50 s after the end of low exercise (second blood sample). By contrast, after the medium- and high-exercise intensity the corresponding decrease in HR was 36.0 ± 6.8 beats·min^{-1} and 35.3 ± 3.5 beats·min^{-1}, respectively. After 5 min of recovery, HR values were still 9.7 ± 2.4 beats·min^{-1} and 16.7 ± 2.1 beats·min^{-1} higher than pre-exercise value respectively.

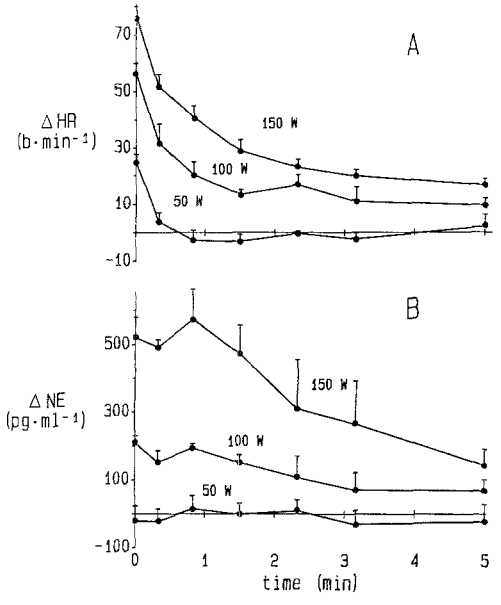

Fig. 2. Increments above resting values in heart rate (*Δ HR*) in **A** and in plasma norepinephrine (*Δ NE*) in **B**, during recovery from low- *(50 W)*, medium- *(100 W)* and high- *(150 W)* exercise intensities. Mean values ± SE

Plasma norepinephrine

Overall mean pre-exercise [NE] was 426.7 ± 23.5 pg·ml^{-1} ($n = 18$). The [NE] values are presented as the difference between actual and pre-exercise value (Δ[NE]) because of the relatively large intra-individual fluctuation of the pre-exercise [NE].

After 5 min of exercise Δ[NE] was -21.0 ± 43.8 pg·ml^{-1} at 50 W, 207.7 ± 22.5 pg·ml^{-1} at 100 W and 521.3 ± 58.3 pg·ml^{-1} at 150 W. The increase above resting is statistically significant at both the medium- and the high-exercise intensity.

In Fig. 2B the mean Δ[NE] values observed during recovery from the three periods of exercise are given. After low-intensity exercise the [NE] fluctuated around the resting value for the entire duration of recovery. After medium- and high-exercise intensity the [NE] decreased from its values during exercise, though not significantly, during the first 20 s of recovery (mean decrease 56.0 ± 28.9 pg·ml^{-1} and 29.0 ± 39.1 pg·ml^{-1}, respectively). Subsequently, after 50 s of recovery from the 100 W exercise the Δ[NE] was 193.9 ± 13.0 pg·ml^{-1}. This is practically the same value as that observed at the end of exercise. After 50 s of recovery from the 150 W load, on the other hand, the Δ[NE] was 547.7 ± 87.5 pg·ml^{-1}, i.e. 52.3 ± 34.5 pg·ml^{-1} higher ($p > 0.05$) than that found at the end of exercise. Thereafter, the [NE] decreased exponentially with τ, calculated from mean Δ[NE], of 87 s at 100 W and 101 s at 150 W. At the 5th min of recovery [NE] values were still 68.2 ± 33.7 pg·ml^{-1} and 142.7 ± 48.9 pg·ml^{-1} higher than pre-exercise values at 100 W and 150 W, respectively.

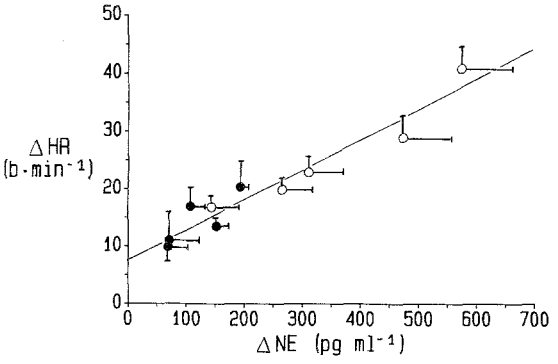

Fig. 3. Increments above resting value in heart rate (*Δ HR*) as a function of the corresponding increments in plasma norepinephrine (*Δ NE*). Each *point* is the average (± *SE*) of the values determined after 50, 90, 140, 190 and 300 s of recovery from the medium- (●) and high- (○) exercise intensity

Heart rate vs norepinephrine

In Fig. 3 the mean ΔHR values observed after 50, 90, 140, 190 and 300 s of recovery (values at 20 s not included) are plotted as a function of the corresponding mean Δ[NE] values for medium- and high-exercise intensity.

The values are related as follows:

$$\Delta HR(beats \cdot min^{-1}) = 0.053\,\Delta[NE](pg \cdot ml^{-1}) + 7.59 \quad (3)$$

$r = 0.96$; $p < 0.05$; $n = 10$.

Discussion

As was observed in previous studies (Davies et al. 1972; Hagberg et al. 1980), the end of submaximal exercise is marked by an exponential decrease in HR toward pre-exercise values.

Our results indicate that after 1 min of recovery from low-exercise intensity, i.e. lower than 33% $\dot{V}_{O_{2max}}$, the HR returns to pre-exercise values with a mono-exponential kinetic. The time constant values are less than 20 s and are similar to those previously reported (Broman and Wigertz 1971; Linnarson 1974). At this exercise intensity there is no significant increase above resting in the plasma [NE], i.e. in sympathetic nervous system activity (Christensen and Brandsborg 1973; Galbo 1983). Thus, the rapid return of HR to resting levels at the end of the exercise is presumably due only to the prompt restoration of vagal activity.

After exercise of an intensity higher than 33% $\dot{V}_{O_{2max}}$, the kinetic of the HR decrement was found to be still mono-exponential, the time constant increasing as the work load increased. Linnarson (1974) observed, on the contrary, a double exponential during the 10-min period following exercise of an intensity higher than 40% $\dot{V}_{O_{2max}}$. However, the reported time constants for the fast component are quite similar to ours and moreover the slow component describes, at most, only 10% of the total ΔHR.

At these same exercise intensities, a significant increase in [NE] was found at the end of exercise indicating that, in addition to the withdrawal of the vagal tone, the activation of the sympathetic system contributed to the increase in HR (Christensen and Galbo 1983; Orizio et al. 1988).

At the 1st min of recovery [NE] either remained constant (medium intensity) or increased (high intensity) with respect to the values found at the end of the task (Fig. 2B). This indicates the persistance of sympathetic activity even after the cessation of an exercise of moderate intensity and short duration and not only after heavy or exhausting tasks, as previously shown (Hagberg et al. 1979; Watson et al. 1980; Dimsdale et al. 1984). It has been suggested that the maintenance of a high [NE] after the cessation of exercise depends on the reflex activation of the sympathetic system elicited by the baroreceptors (Watson et al. 1980; Dimsdale et al. 1984).

In spite of the persistent sympathetic activity after 100 W and 150 W exercise, the HR decreased in the 1st min of recovery by about 35 beats$\cdot$min^{-1} (Fig. 2A). This value is similar to the increment in HR found at the very onset of exercise which is attributable to the withdrawal of vagal tone (Christensen and Brandsborg 1973; Orizio et al. 1988). The prompt decrease in HR observed at the end of exercise could, therefore, be due to the restoration of the activity of the same drive, i.e. the restoration of vagal tone.

After a time lag of 1 min, the [NE] decreases exponentially, reflecting the return of sympathetic activity to basal values (Galbo 1983). We found that the time constant of the [NE] decrease is longer, the higher the intensity of exercise. This is not in agreement with Hagberg et al. (1979) who showed that the disappearance of [NE] is approximately the same at different work loads. However, these authors investigated only exercise intensities higher than 80% $\dot{V}_{O_{2max}}$.

The reduction of [NE] is coupled with a further decrease in HR (Figs. 2, 3). It is evident from Eq. 3 that a decrease of 100 pg$\cdot$ml^{-1} in [NE] is accompanied by a decrease of about 5 beats$\cdot$min^{-1} in HR. This ratio is practically the same as that found in the transition from rest to exercise, when allowance is made for the withdrawal of vagal tone (Orizio et al. 1988). Therefore by analogy, it could be hypothesized that the decrease in HR, after the initial rapid drop of 35 beats$\cdot$min^{-1}, could depend on the progressive attenuation of sympathetic activity.

In conclusion, it appears that during the 1st min of recovery the para-sympathetic system is the major effector in reducing HR, independent of exercise intensity. At work loads higher than about 30% $\dot{V}_{O_{2max}}$ the return of HR to the pre-exercise value depends also on the gradual reduction of activity in the sympathetic system.

Acknowledgements. This work was partially supported by Istituto di Tecnologie Biomediche Avanzate, Physiology Section, Consiglio Nazionale delle Ricerche, Milan, Italy and by Ministero delle Pubblica Istruzione, Italy.

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Accepted January 3, 1989