Abstract We tested the hypothesis that, in healthy middle-aged subjects (n=11, age 51.0±3.0 years, x±SD), the effects of exercise training on pulmonary O₂ uptake (VO₂) on- and off-kinetics would appear earlier than those on peak VO₂. The subjects underwent a standard training program (combined endurance and resistance training) in a health club, and were evaluated before training ("time 0", T0), and after 7 (T7), 15 (T15), 30 (T30), 60 (T60) and 90 (T90) days of training. Breath-by-breath pulmonary O₂ uptake (VO₂), heart rate (HR), systolic (SBP) and diastolic blood pressure, and capillary blood lactate concentration ([La]b) were determined at rest and at each workload (w) during a cycle ergometer incremental exercise test. The "heart rate · blood pressure product" was calculated as (HR·SBP). The day following the incremental test, the subjects performed three repetitions of a square-wave exercise at 50% of VO₂peak, for the determination of pulmonary VO₂ on- and off-kinetics. VO₂peak and [La]bpeak tended to increase with training; the increases became significant at T60 or T90. HRpeak and (HR·SBP)peak were unaffected by training. The time constant of the "primary" component of the VO₂ on-kinetics (τ₂) was 46.9±17.3 s (T0), 38.1±14.2 s (T7), 34.4±12.6 s (T15), 28.8±6.8 s (T30), 30.2±8.0 s (T60), and 30.4±12.4 s (T90); a significant difference compared to T0 was observed from T15 onward. From T15 onward, τ₂ were not significantly different from values obtained (29.2±5.3 s) from a group of healthy untrained young controls (n=7, 21.6±0.5 years). The same pattern of change as a function of training was described for the VO₂ off-kinetics. It is concluded that in 50-year-old subjects VO₂ on- and off-kinetics are more sensitive to exercise training than other physiological variables determined at peak exercise.

Keywords Aging · Oxygen uptake kinetics · Training

Introduction

Upon a step transition from rest to exercise, the rate of increase of oxygen uptake (VO₂) is slower than that of power output, and follows a time-course often termed VO₂ on-kinetics. Pulmonary VO₂ on-kinetics, as usually determined in a clinical setting or in the exercise physiology laboratory, matches rather closely the on-kinetics of VO₂ directly determined across exercising limbs [14]. More specifically, the "primary" component, or "phase 2", of pulmonary VO₂ on-kinetics should closely reflect the kinetics of adjustment of oxidative metabolism at the skeletal muscle level [24]. It is generally agreed that a "metabolic inertia" within muscles during transitions to low-intensity exercise is the main limiting factor for VO₂ on-kinetics [7, 13, 23]. VO₂ on-kinetics during cycling exercise is known to get progressively slower with age [3, 4, 8, 9, 11]. Decreases in the rate of adjustment of skeletal muscle oxidative metabolism to increases in work rate increase the need for substrate-level phosphorylation and cause a greater disturbance of cellular and organ homeostasis; this has obvious implications for exercise capacity and muscle fatigue. The effects of endurance training on VO₂ on-kinetics in young subjects are known to occur very early (after 4 days of training), well before changes in maximal oxygen uptake (VO₂max) are observed [18]. It is also known that a 6-month endurance training program in aged subjects (≥70 years old) results in faster VO₂ on-kinetics [2]. To
our knowledge, no data are available on the time-course of the effects of exercise training on \( \dot{V}O_2 \) kinetics in middle-aged and old subjects. Should the response be similar to that of young subjects [18], the positive effects of exercise training in middle-aged and old subjects would also become manifest after relatively short training programs, before changes in other physiological variables (such as \( \dot{V}O_2_{\text{max}} \)) could appear. We tested this hypothesis in the present study. This was conducted on a group of middle-aged (\( \geq 50 \)-year-old) previously untrained healthy subjects, undergoing a 3-month standard training program (including both “aerobic” and “resistance” training) in a health club, following the guidelines recommended by the American College of Sports Medicine (ACSM) [1]. The subjects were tested at different times during the program, in order to allow the investigators to detect possible early effects of exercise training on \( \dot{V}O_2 \) on- and off-kinetics, as well as on other physiological variables determined during submaximal constant-load bicycle exercise and during incremental bicycle exercise to exhaustion.

Materials and methods

Subjects

The study was conducted on 11 healthy previously untrained middle-aged males (\( \text{age} 51.0 \pm 3.0 \text{ years} \) (\( \pm \text{SD} \)), height 176.9 \pm 5.6 cm, body mass 86.0 \pm 11.8 kg, BMI 27.3 \pm 2.5). For reference, a group of young healthy untrained males (YG) (medical school students, \( n=7; \text{age} 21.6 \pm 0.5 \text{ years} \), height 176.1 \pm 7.8 cm, body mass 72.1 \pm 5.4 kg, BMI 23.3 \pm 1.5) was also tested. The subjects were fully informed of any risks and discomforts associated with these experiments before giving their written, informed consent to participate in this study, which was approved by the ethics committee of the Institutional Review Board of Istituto di Tecnologie Biomediche Avanzate, Consiglio Nazionale delle Ricerche, Milan, Italy.

Training program

Middle-aged subjects underwent a 90-day standard training program. The subjects trained three times a week, and each training session included, after some warm-up exercises, 30 min of cycle exercise at a workload corresponding to \( \geq 50\% \) of the difference between resting heart rate and peak heart rate (determined during the incremental exercise, see below), as well as 30 min of “resistance” (strength) training [six different exercises involving the major muscle groups of the upper and lower limbs, with 12–15 repetitions of each exercise at \( \geq 70\% \) of one repetition maximum (1RM) determined serially during the training period], according to a standard protocol utilized in the club and recommendations by ACSM [1]. Training sessions were supervised closely by experienced personnel. YG did not undergo any training program.

Exercise protocols

All tests were carried out under close medical supervision, and the subjects were continuously monitored by 12-lead electrocardiography (ECG). The tests were carried out in the afternoon, a few hours after a light meal. Ambient temperature in the laboratory was kept at \( \leq 20^\circ\text{C} \) (relative humidity 55–60%). Before training (T0) and 7 (T7), 15 (T15), 30 (T30), 60 (T60) and 90 (T90) days after the beginning of the training program the subjects underwent an incremental bicycle exercise (incremental exercise: starting from rest, 30 W added every 3 min) to voluntary exhaustion, which was defined as the inability to sustain the recommended pedaling frequency of \( \geq 60 \) revolutions/min despite vigorous encouragement by the operators. An electromagnetically braked cycle ergometer (Cardioline STS 3) was utilized. Pedaling frequency was digitally displayed to the subjects throughout the tests.

The day following the incremental test, the subjects performed three repetitions of a square-wave exercise (constant load exercise) on the same bicycle ergometer, at a workload corresponding to 50% of \( \dot{V}O_2_{\text{peak}} \). Pedaling frequency was kept at \( \geq 60 \) revolutions/min. At least 10–15 min of rest was observed between repetitions. On-transitions were from rest (subjects sitting on the cycle ergometer, with feet tightly strapped to the pedals) to the imposed load, which was attained in \( \pm 3 \text{ s} \). Off-transitions were from the imposed load to rest. Orders to start and stop pedaling were given by voice to the subjects, without warning.

Investigated variables

Pulmonary ventilation (\( \dot{V}E \)), \( \dot{V}O_2 \), and \( \dot{CO}_2 \) output (\( \dot{V}CO_2 \)) were determined breath-by-breath by a computerized metabolic cart (Sensor Medics Vmax29c). Expiratory flow measurement was performed by a mass flow sensor (hot wire anemometer), calibrated before each experiment by a 3-liter syringe at three different flow rates. Tidal volume (\( \dot{V}T \)) and \( \dot{V}E \) were calculated by integration of the flow tracings recorded at the mouth of the subject. \( \dot{V}O_2 \) and \( \dot{V}CO_2 \) were determined by continuously monitoring \( P_O_2 \) and \( P_CO_2 \) at the mouth of the subject throughout the respiratory cycle and from established mass balance equations, after alignment of the expiratory volume and expiratory gases tracings and A/D conversion. Calibration of the \( O_2 \) and \( CO_2 \) analyzers was performed before each experiment by utilizing gas mixtures of known composition. Digital data were transmitted to a personal computer and stored on disk. \( \dot{V}O_2 \) and \( \dot{V}CO_2 \) were expressed in STPD, \( \dot{V}E \) in BTPS. The gas exchange ratio (\( \dot{R} \)) was calculated as \( \dot{V}CO_2/\dot{V}O_2 \).

Heart rate (HR) was determined beat-by-beat from the \( R–R \) intervals by a heart rate coupler (PE4000, Polar Electro). Systolic (SBP) and diastolic blood pressures were determined during the last 30 s of each step of the incremental test by a sphygmomanometer. The HR-SBP product (taken as an indication of cardiac work) was also calculated. The YG group did not have their blood pressure measured. Arterial blood \( O_2 \) saturation (\( SaO_2 \)) was continuously monitored by pulse oximetry (Biox 3740 Pulse Oximeter, Ohmeda) at the earlobe.

At rest, during the last 30 s of each step of the incremental test and at different times during the first minutes of recovery after the incremental and the constant load tests, 20 \( \mu l \) of earlobe capillary blood was obtained for the determination of lactate concentration (\( [Lact]_e \)) by an enzymatic method (ESAT 6661 Lactat, Eppendorf).

Data analysis

Steady-state values of \( \dot{V}E \), \( \dot{V}O_2 \), \( \dot{V}CO_2 \), \( SaO_2 \), and HR for each workload of the incremental test were obtained by calculating averages of breath-by-breath or beat-by-beat values over the last 30–40 s of each workload. Resting values were obtained by calculating averages during \( \leq 1 \text{ min} \) of rest. Values obtained during the last 30 s of the incremental exercise were considered “peak” values.

As for the constant load exercise, breath-by-breath \( \dot{V}O_2 \) data and beat-by-beat HR data obtained during the three repetitions were time-aligned and superimposed for each subject. Resting and steady-state values were calculated over a 1-min interval at rest, during the last minute of exercise, and between the 4th and 5th