NASA-CR

FIRST ANNUAL STATUS REPORT
PROJECT NAGW-4359

TO:

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
SPACE BIOMEDICAL SCIENCES

“CO_2-O_2 INTERACTIONS IN EXTENSION OF TOLERANCE TO ACUTE HYPOXIA”

(Period 1 April, 1995 to 31 March, 1996)

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FIRST ANNUAL STATUS REPORT: PROJECT NAGW-4359 "CO_2-O_2 INTERACTIONS IN EXTENSION OF TOLERANCE TO ACUTE HYPOXIA"

Highlights of the Previous Project (NAG9-597) ("CO_2-O_2 Interactions in Extension of Tolerance to Acute Hypoxia").

The goals of the Previous Project were (a) to establish sensitive indices of mental and psychomotor performance in exposures to graded degrees of stable states of acute hypoxia at rest and (b) to use the selected indices for determination of the degrees of performance decrement produced by hypoxia alone, and hypoxia with normocapnia.

The purposes were accomplished for stable states of atmospheric hypoxia, both at rest and in graded exercise.

Emphasis in the Project was also on methods development for subsequent use in dynamic conditions, as well as stable degrees of hypoxia, and hypercarbia.

The IFEM developed computer-controlled Performance Measurement System greatly facilitated a search for sensitive measures of hypoxic effects on mental performance with inspired O_2 concentrations of 12% and 10%. Of ten Tests evaluated in several experimental series, two (Word-number Test of Associative Memory Ability and Division Test of Numerical Ability) always showed large and significant decrements with 10% inspired O_2. Sizeable and significant reductions in test scores during exposure to 10% O_2 were reversed when 4.1% CO_2 was added to the hypoxic inspired gas. Simultaneous physiological measurements included ventilation, end-tidal PO_2 and PCO_2, arterial O_2 saturation and heart rate, but measurement of middle cerebral artery blood flow velocity was not yet available.

Velocity of blood flow in the middle cerebral artery (MCA vel) was calibrated against the ^{133}Xenon method of brain blood flow determination over a wide range of arterial PCO_2. Methods were developed for reliable measurement of MCA vel under water while exercising. In immersion (partial simulation of acute exposure to null gravity) during graded exercise, and during graded increments of arterial PCO_2, calibrated MCA vel and ventilation were not different when measured under the dry condition, in partial immersion to the neck, or in total immersion.

Goals of the Present Project Year (NAGW 4359) (Summary).

The investigations of the Present Project year have continued as one component of an overall Program concerned with advantageous and/or detrimental influences associated with purposeful deviations from atmospheric levels of O_2 and CO_2. One Program component with Navy Medical Research and Development Command support relates to extension of CNS tolerance to *hyperoxia* and prevention of deleterious rise in P_aCO_2 during exercise. The current NASA component relates to purposeful elevation of P_aCO_2 to accomplish acute adaptation to inspiratory *hypoxia*. The overall Program continues in intimate relationship to the analysis, modeling, and data preservation objectives of NAGW-3628: "Environmental Biomedical Research Data Center" (Aerospace, Atmospheric, Undersea).

Specific goals of the present year have been directed to simulating situations of emergency or accidental exposure to hypoxic (10% O_2) environments. They included establishing dynamic effects of hypoxia with and without CO_2 (rate of acute adaptation), and stable-state (equilibrium) effects on blood and brain oxygenation. They also included effects on the physiological parameters of respiration and blood gas composition which underlie brain oxygenation.

Current Accomplishments.

Measurement of Circulatory Parameters.

Following development of a dependable method of stabilizing the transcranial ultrasonic doppler probe during exercise as well as during prolonged periods at rest, reliable measurement of middle cerebral artery blood flow velocity was added to the physiological parameters previously obtained. Determination of cardiac output by impedance cardiography was also added, to supplement heart rate as an indicator of relative cardiac responses.

Comparative Dynamic and Equilibrium Responses of Brain Oxygen Flow Rate to Abrupt Exposures to Inhaled 10% O_2 and 10% O_2/4% CO_2 at Rest, Followed by 50 and 100 Watts Exercise.

Seven subjects completed the multiple experiment protocols as outlined in Appendix Fig. A1. Prior to the experiment day, prospective subjects were tested for their ability to complete the exercise protocol, and to familiarize them with the experimental circumstances.

For 10% O_2, a complete experiment consisted of three identical rest-exercise phases of 32 min. duration (Fig. A1). Following a five minute air control period, each inspired gas was administered over the next 27 minutes. The test gases were room air control, 10% ± 0.1% O_2 with 4% ± 0.1% CO_2, and 10% ± 0.1% O_2. A minimum of 45 minutes separated each phase.

Interactions.

Brain oxygenation depends in part on flow rate of oxygen in brain arterial blood (QO_2) (Fig. A2) e.g. supply of oxygen available for diffusion. Flow rate of oxygen is calculated as the product of arterial oxygen content ($[O_2]$) (Fig. A3) and brain blood flow rate (CBF) (Fig. A4). Oxygen content is here calculated as the product of arterial O_2 saturation by continuous pulse oximetry (S_aO_2) (Fig. A5) and 20.0 vols. % blood O_2 capacity. Continuous CBF is estimated from calibrated middle cerebral artery blood flow velocity. The dynamic response of QO_2 to change in environmental O_2 and CO_2 is complex, since the two control systems for ventilation and the control of CBF are coupled and interact through the arterial respiratory blood gases. Thus, the dynamic response of CBF is a function of arterial PO_2 (Fig. A6 - $P_{ET}O_2$) and PCO_2 (Fig. A7- $P_{EST.\,ART}CO_2$), as is the dynamic response of ventilation. Ventilation in turn interacts dynamically with the blood gases and S_aO_2, and therefore with CBF. The description of dynamic responses which follows is necessarily here limited to QO_2, and is in terms of time for a response to change one-half of the way from one state to another ($T_{1/2}$).

Figs A2-A7 are plots of the parameters cited above against time for each of the three experiment phases. Results for other physiological parameters are not presented in this report, except for cardiac output (below).

Changes in QO_2 During Transitions from Air to 10% O2 and 10% O_2 with 4% CO_2 at-Rest.

At zero time, transition is abruptly made from air at-rest to the experimental gas at-rest. As shown in Fig. A2 for 10% O_2 inspired, after a minute or so, QO_2 decreases with $T_{1/2}$ of about 45 sec. to about 17% below its initial level at 2 min. QO_2 remains below control throughout the remainder of the 10 min. rest period, varying between 16% and 20% below. The decline in QO_2 persists despite an increasing CBF (Fig. A4) due to a marked fall in $[O_2]$ (Fig. A3). In contrast, for 10% O_2 with 4% CO_2, QO_2 initially increases to a local peak value 12% above control with $T_{1/2}$ of about 15 sec., and remains between 4% to 12% above control the remainder of the rest period. The increment in QO_2 is due to an attenuated decline in $[O_2]$ and increment in CBF (Figs. A3 and A4). As expected, QO_2 during air control fluctuates slightly about a stable level.

Changes in QO_2 During Transitions From Rest to 50 Watts Exercise.

In transition from rest to 6 min. of 50 Watts ergometer exercise while breathing 10% O_2, QO_2 transiently dropped to a trough from 16% below control to 20% below. then rose to a peak value 9% below control 1.5 min. after exercise onset with $T_{1/2}$ of about 30 sec. It then settled to about 11% below control. Again in contrast, QO_2 for 10% O_2 with 4% CO_2 increased from 12% above control to a stable 37% above control, with $T_{1/2}$ about 1 min. This occurred despite a decline in $[O_2]$ due to a marked rise in CBF. During air control, QO_2 increased somewhat to a new stable level due to an increment in CBF associated with the expected small increase in P_aCO_2 (Fig. A7) which accompanies light exercise.

Changes in QO_2 During Transitions From 50 Watts to 100 Watts.

Abrupt increase in the degree of imposed exercise from 50 Watts to 100 Watts resulted in little further change in QO_2 while 10% O_2 was inspired, but led to a large further rise while 10% O_2 with 4% CO_2 was inspired, increasing almost linearly with time, peaking at 54% above control.

Summary.

Relative to inspiration of 10% O2, brain oxygenation is enhanced by addition of 4% CO_2 to the inspired 10% O_2 . This is accomplished by increasing the rate at which O_2 in arterial blood is supplied to the brain circulation (well above even the normoxic level), and on relative improvement in the arterial pressure of O_2 (Figs. A2 and A6).

For the ultimate description of brain-oxygenation, improvement of dynamic measurement of arterial PO_2 is required, to replace the present measurements, of end-tidal PO_2

Cardiac Output.

Fig. A8 shows cardiac output as determined during the final min. of each rest and exercise period. As with heart rate (not shown here), cardiac output was consistently less when the O_2/CO_2 mixture was breathed than when 10% O_2 by itself was inspired, indicating a lesser degree of hypoxic cardiac stress.

Acquisition and Integration of a Digital Data Acquisition/Analysis System.

A highly flexible multi channel digital data acquisition system (DATAQ Instruments DI-220PGH) with acquisition (WINDAQ/200), playback-data reduction (WINDAQ/EX) and advanced data processing (ADVANCED CODAS) software has been acquired and is being customized for integration into the Program's measurement and data analysis systems. All data files will then be stored in digital form on magnetic media, and data reduction and processing will be with the aid of and in the realm of computer software. The large data files generated during data acquisition will conveniently be transferred among computers linked by the Environmental Biomedical Research Data Center local area network for data reduction, analysis, and storage.

Plans for the Coming Year.

Initial Plans for experiment and methods development during the forthcoming year include:

Quantitative Dynamic Comparisons of changes in respiration and brain blood flow, and lung, blood and brain oxygenation, in abrupt transitions from normoxic states of rest, and states of moderate exercise activity to 12, 10 and 8% oxygen at one atmosphere.

Use of selected rapid response psychometric test for comparison of the time course of performance change in relation to computed internal carbon dioxide and oxygen pressures.

The general purpose is stepwise investigation of accelerated adaptation to stepwise increases in hypoxic stress, through optimal use of carbon dioxide and natural control mechanisms.

APPENDIX

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Reports and Publications - current report period.

Gelfand, R., and G. Beck, Jr. Transcranial doppler adaptation to monitor MCA blood velocity during immersion and dry conditions while exercising and at rest. (Abstract). Accepted, *Undersea & Hyperbaric Med.* In Press (Spring, 1996).

Clark, J.M., C.J. Lambertsen, R. Gelfand, and E.J. Hopkin. Analysis of factors that determine rates of recovery from human pulmonary oxygen poisoning in Predictive Studies V. (Abstract) Accepted, *Undersea & Hyperbaric Med.* In Press (Spring, 1996).

Gelfand, R., C.J. Lambertsen, G. Beck, Jr., and J.M. Clark. Dynamic responses of S_aO_2 and "CBF" to abrupt exposure to inhaled 10% O_2 / 4% CO_2 at rest, followed by 50 and 100 watts exercise. (Abstract). *Undersea & Hyperbaric Med.*, 22 (S): 70-71, 1995.

Clark, J.M., R. Gelfand, C.J. Lambertsen, W.C. Stevens, G. Beck, Jr., and D.F. Fisher. Human tolerance and physiological responses to exercise while breathing oxygen at 2.0 ATA. *Aviat. Space Environ. Med.* 66: 336-45, 1995.

Clark, J.M., R. Gelfand, C.J. Lambertsen, G. Beck, Jr., and K.R. Hardy, Ventilatory, arterial PCO_2, and cerebral circulatory responses to incremental exercise during O_2 breathing at 2.0 ATA.
(Abstract). *Undersea & Hyperbaric Med.*, 22 (S): 69-70, 1995.

Figures A1 through A8 are on following *APPENDIX* pages.

Fig. A1

EXPERIMENT PROTOCOL FOR PHYSIOLOGICAL RESPONSES TO 10% O_2 AND 10% O_2 / 4% CO_2 IN REST AND EXERCISE

Inspired Gas

Air Control
10% O_2 / 4% CO_2
10% O_2 / Bal. N_2

Ergometer-Imposed Workloads

Exercise 1	50 Watts
Exercise 2	100 Watts

@ 60 rpm

Measurements:

TCD-MCA, V_E, V_T, f,SaO_2
P_{ET} CO_2,P_{ET} O_2,HR,CO

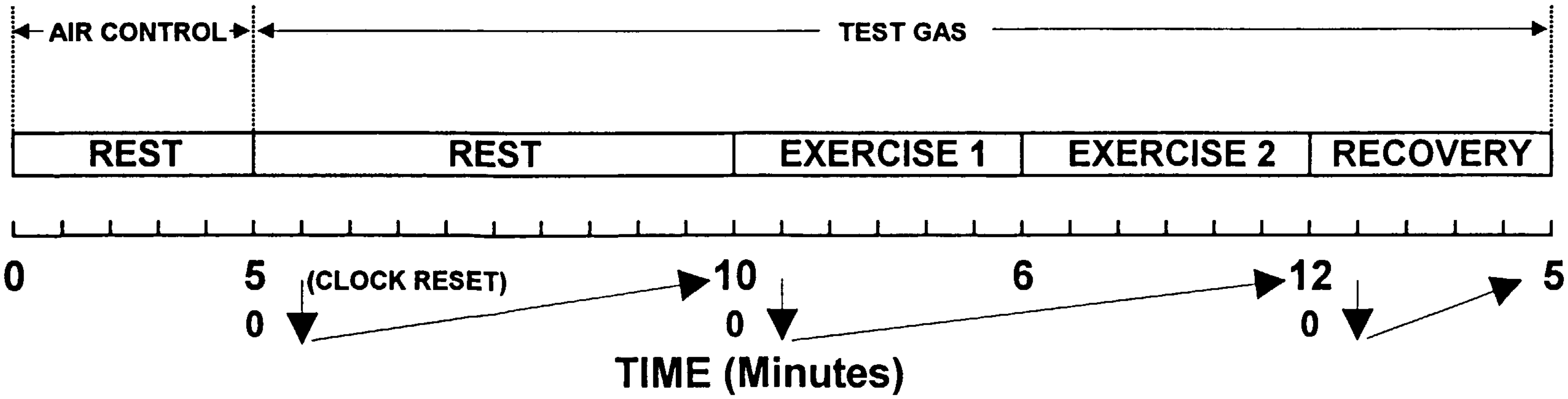

Fig. A2
DYNAMIC CHANGES IN "BRAIN OXYGEN FLOW RATE"
FOLLOWING INSPIRATION OF 10% O_2 AND 10% O_2 WITH 4% CO_2
AT REST FOLLOWED BY 50 AND 100 WATTS EXERCISE
Mean ± SEM, N = 7

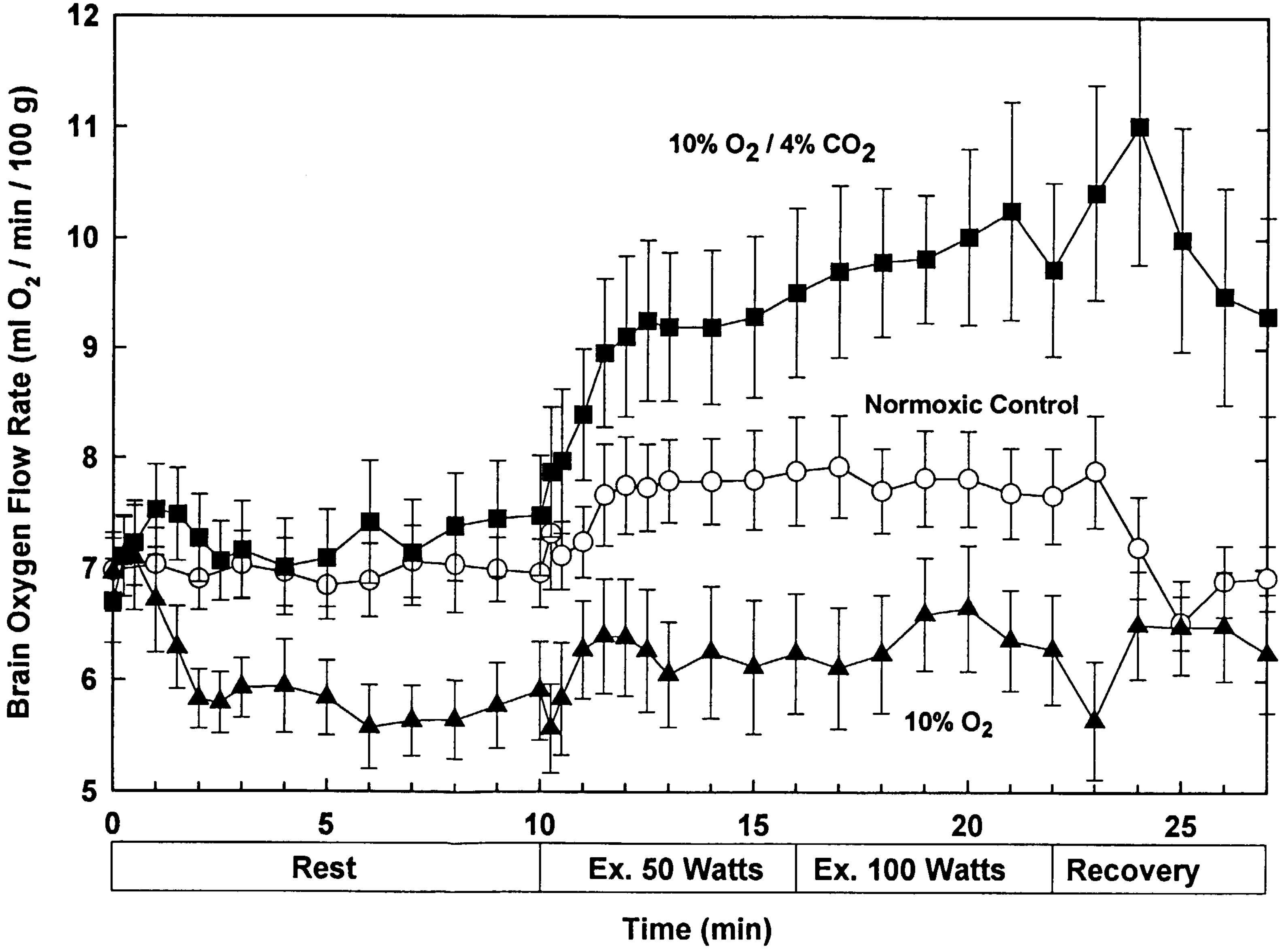

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Fig. A3

DYNAMIC CHANGES IN ARTERIAL OXYGEN CONTENT FOLLOWING INSPIRATION OF 10% O_2 AND 10% O_2 WITH 4% CO_2 AT REST FOLLOWED BY 50 AND 100 WATTS EXERCISE

Mean ± SEM, N = 7

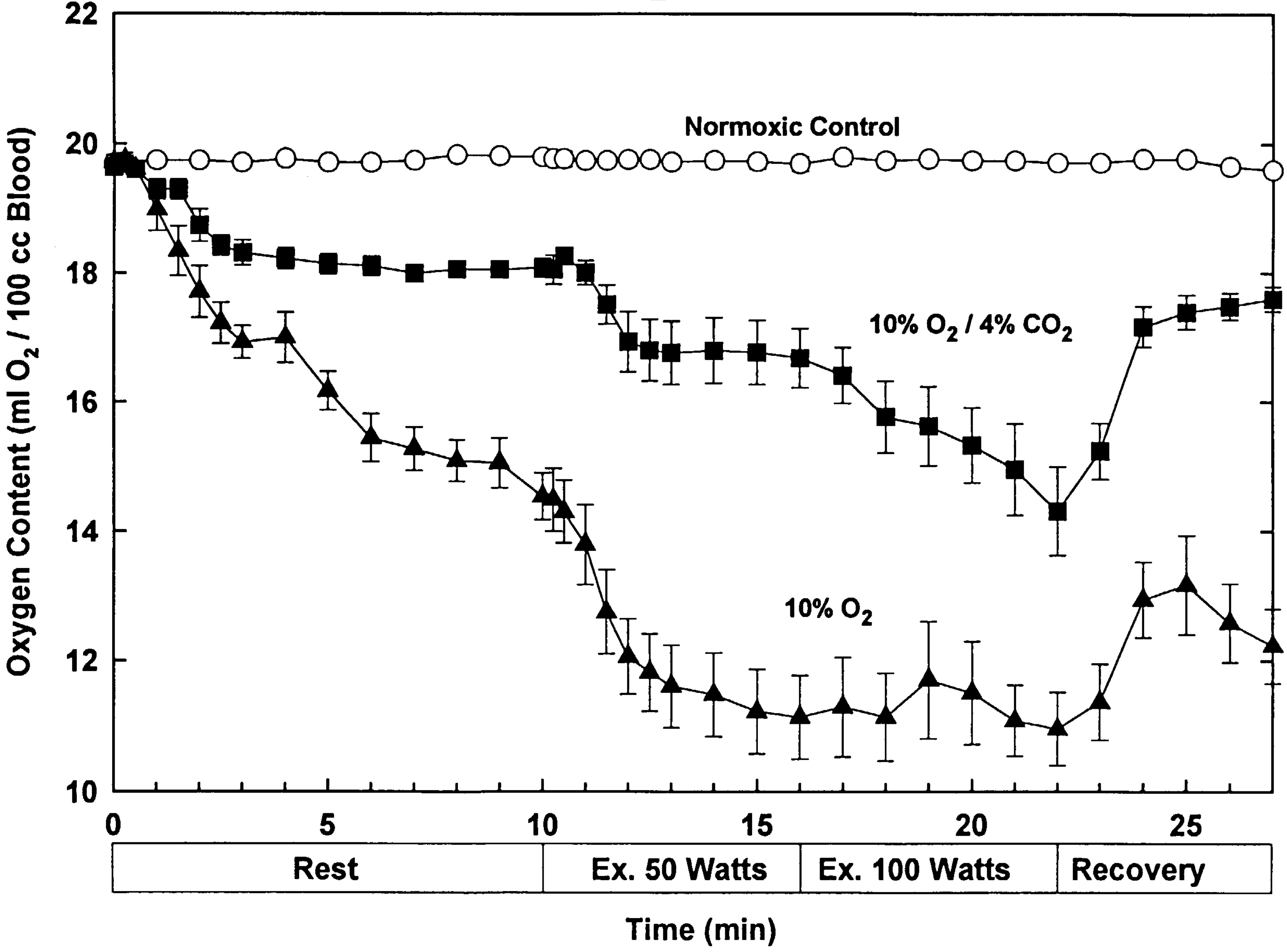

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Fig. A4

DYNAMIC CHANGES IN "BRAIN BLOOD FLOW"
FOLLOWING INSPIRATION OF 10% O_2 AND 10% O_2 WITH 4% CO_2
AT REST FOLLOWED BY 50 AND 100 WATTS EXERCISE

Mean ± SEM, N = 7 Subjects

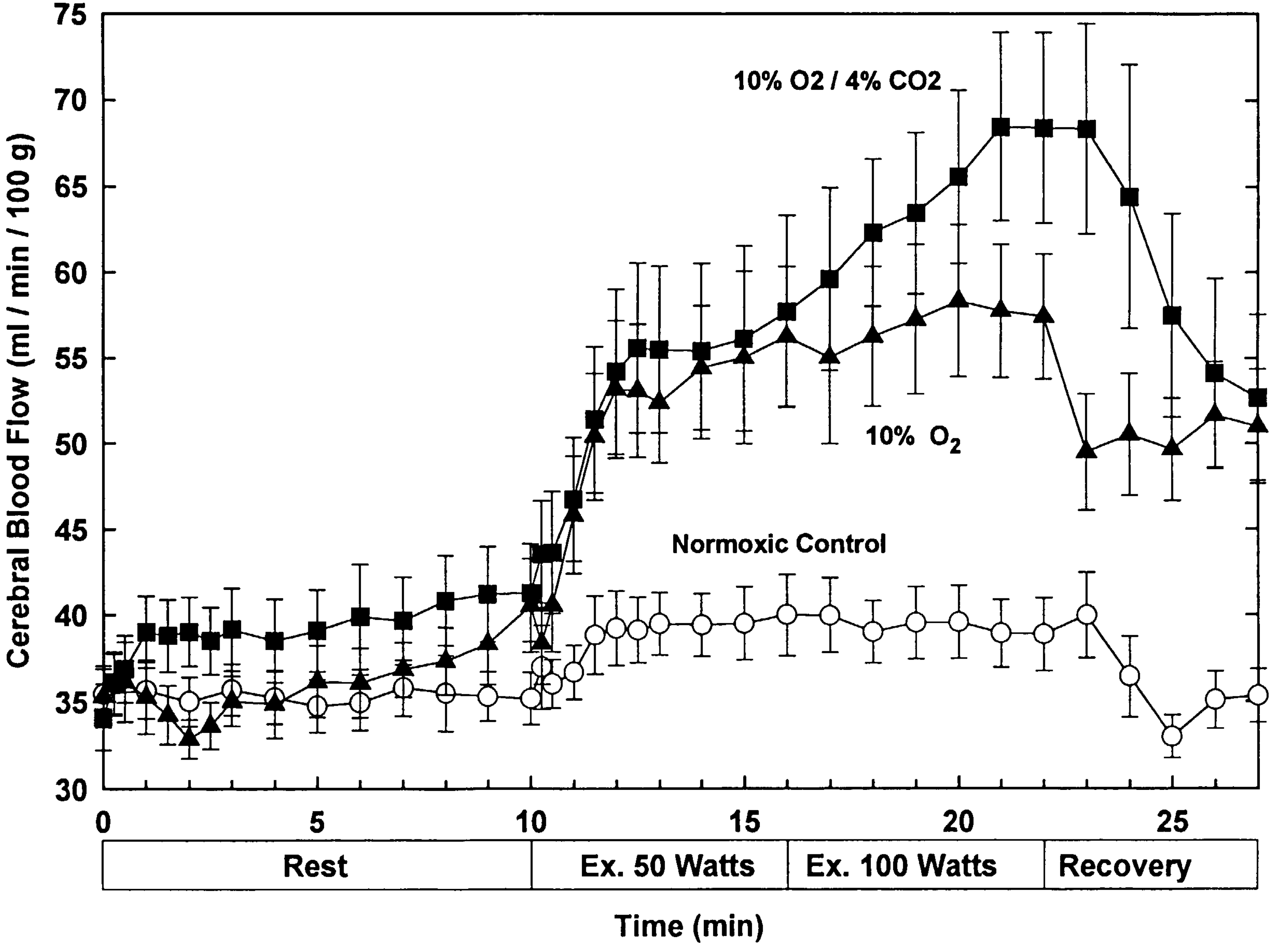

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Fig. A5

DYNAMIC CHANGES IN ARTERIAL OXYGEN SATURATION FOLLOWING INSPIRATION OF 10% O_2 AND 10% O_2 WITH 4% CO_2 AT REST FOLLOWED BY 50 AND 100 WATTS EXERCISE

Mean ± SEM, N = 7

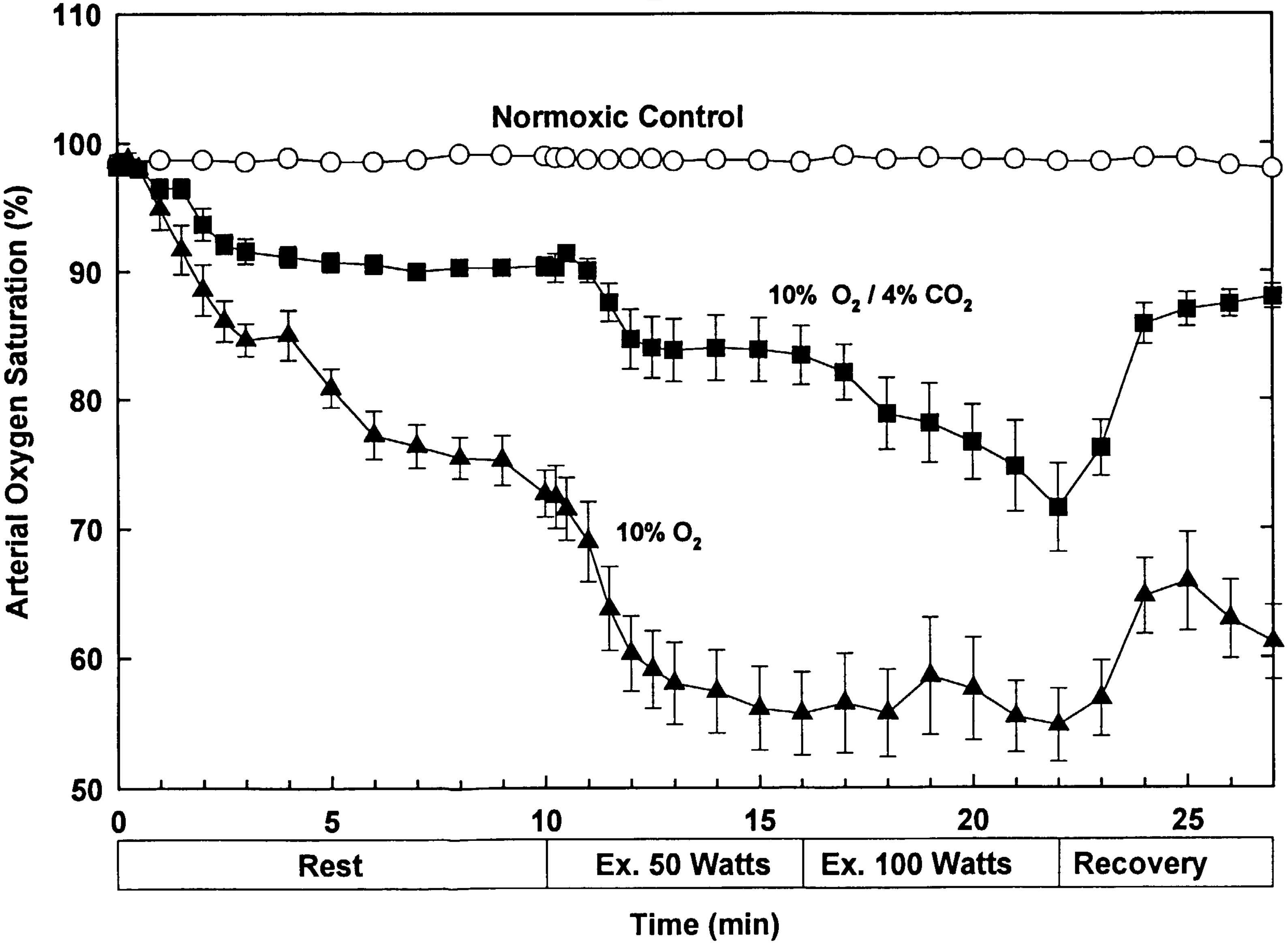

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Fig. A6

DYNAMIC CHANGES IN END-TIDAL OXYGEN TENSION FOLLOWING INSPIRATION OF 10% O_2 AND 10% O_2 WITH 4% CO_2 AT REST FOLLOWED BY 50 AND 100 WATTS EXERCISE

Mean ± SEM, N = 7

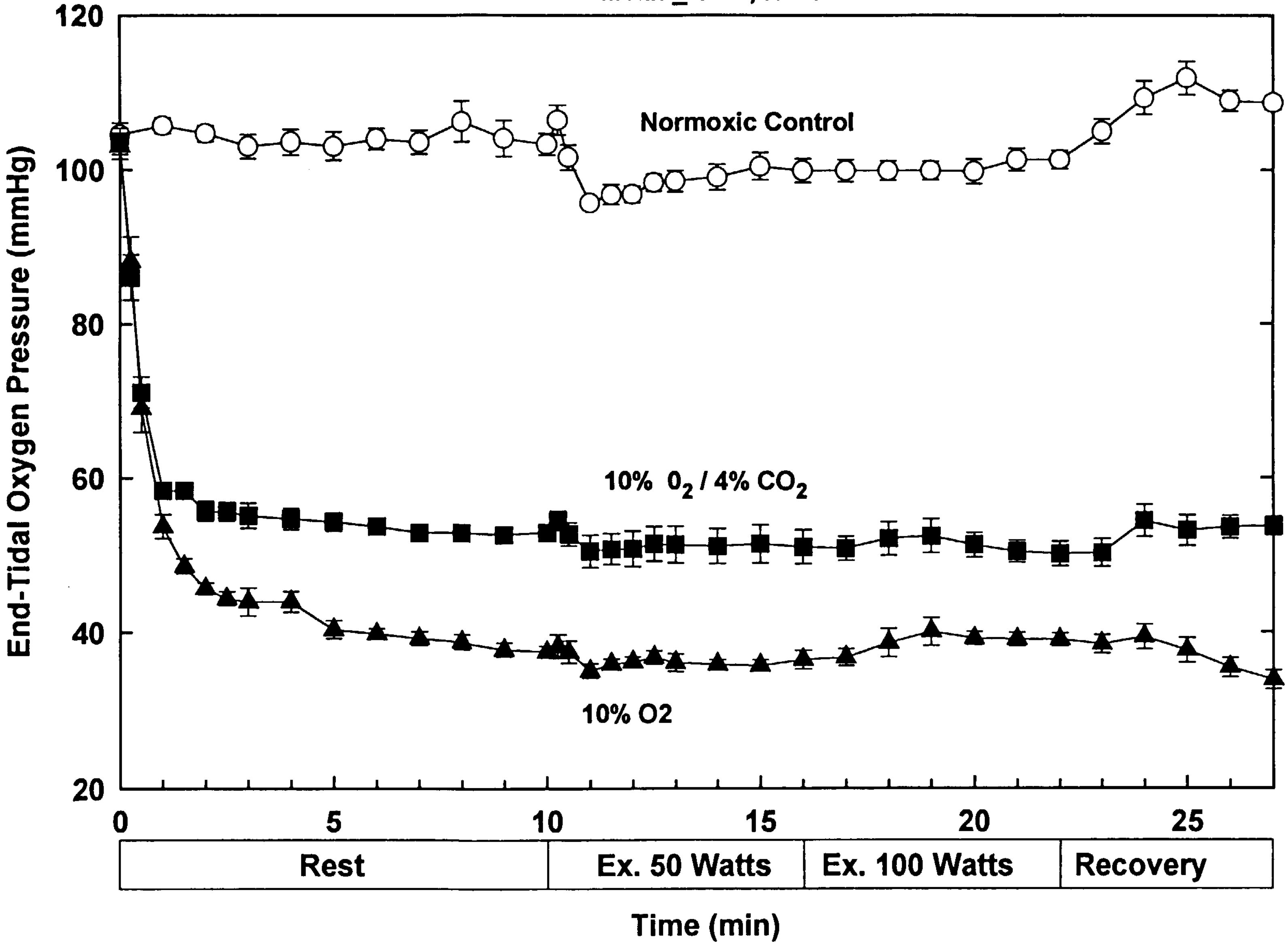

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Fig. A7

DYNAMIC CHANGES IN ESTIMATED ARTERIAL CARBON DIOXIDE TENSION FOLLOWING INSPIRATION OF 10% O_2 AND 10% O_2 WITH 4% CO_2 AT REST FOLLOWED BY 50 AND 100 WATTS EXERCISE

Mean ± SEM, N = 7

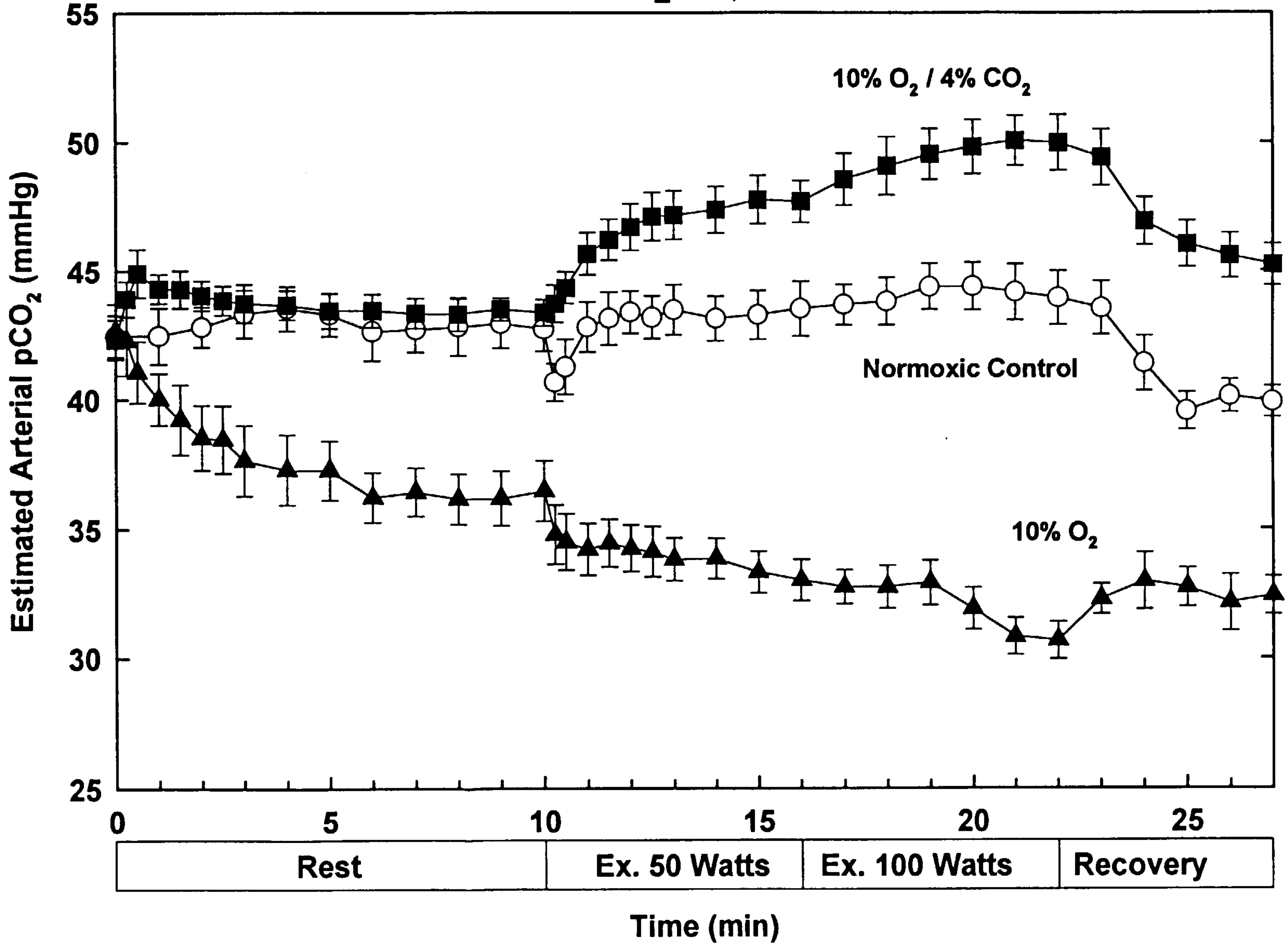

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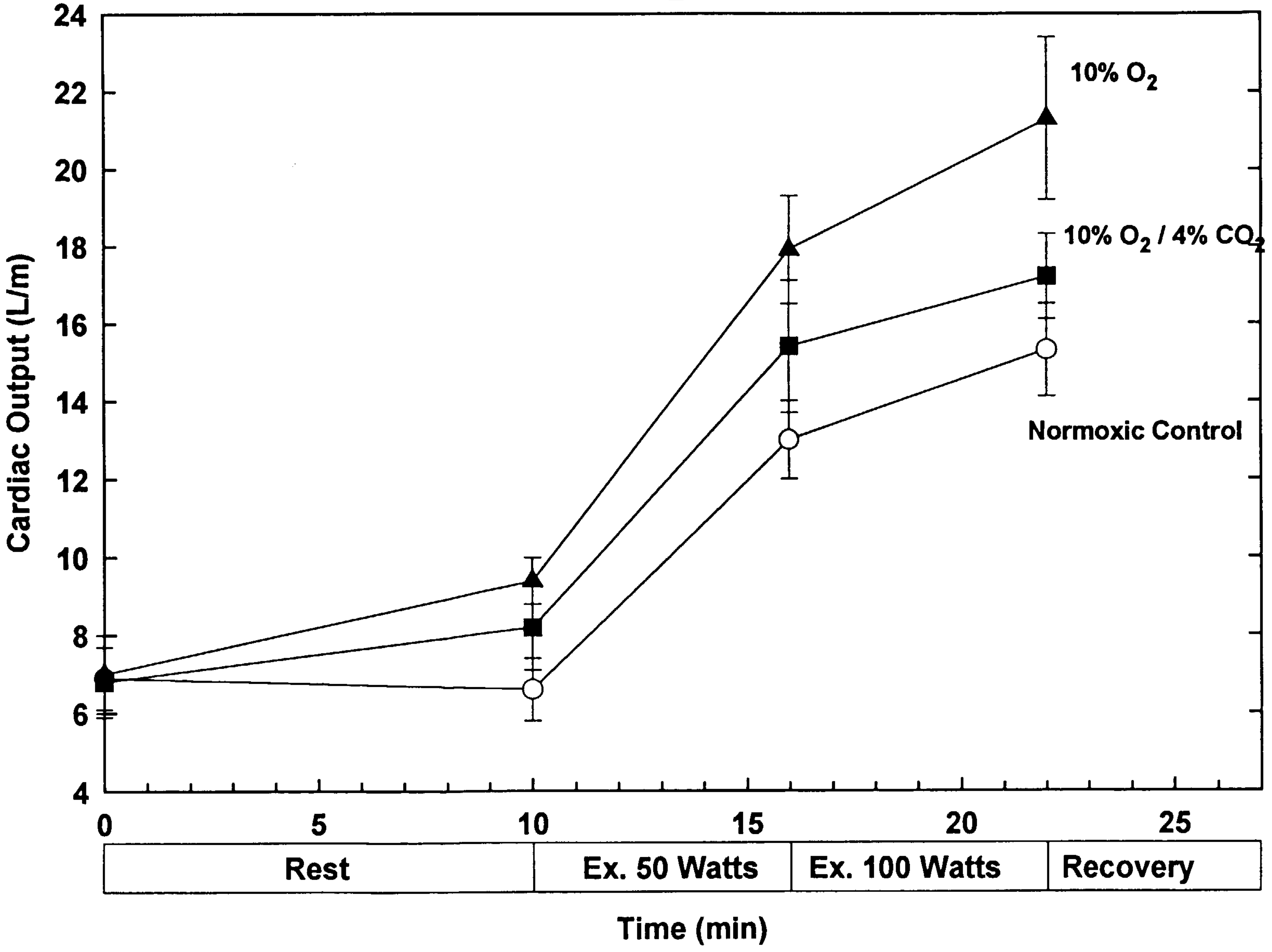
Fig. A8

CARDIAC OUTPUT CHANGES AFTER INSPIRATION OF 10% 0_2 AND 10% O_2 WITH 4% CO_2 DURING REST AND EXERCISE AT 50 and 100 Watts

Mean ± SEM, N = 7



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