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EXERCISING WITH RESERVE: Evidence that the CNS regulates prolonged exercise performance.

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Abstract

Objective: The purpose of this study was to measure the effects of an amphetamine (methylphenidate) on exercise performance at a fixed rating of perceived exertion of 16
Methods: Eight elite cyclists ingested 10mg Methylphenidate in a randomized, placebo-controlled cross-over trial.
Results: Compared to placebo, subjects receiving methylphenidate cycled for ~ 32% longer before power output fell to 70% of the starting value. At the equivalent time at which the placebo trial terminated, subjects receiving methylphenidate had significantly higher power outputs, oxygen consumptions, heart rates, ventilatory volumes and blood lactate concentrations although EMG activity remained unchanged. Thus the ingestion of a centrally-acting stimulant allowed subjects to exercise for longer at higher cardio-respiratory and metabolic stress indicating the presence of a muscular reserve in the natural state.
Conclusions: This suggests that endurance performance is not only "limited" by mechanical failure of the exercising muscles ("peripheral fatigue"). Rather performance during prolonged endurance exercise under normal conditions is highly regulated by the CNS to insure that whole body homeostasis is protected and an emergency reserve is always present.

A central debate in the exercise sciences is the nature of the fatigue that determines exercise performance under different conditions.

Two opposing theories are currently popular. The first holds that exercise is limited principally by metabolic changes in the exercising skeletal muscles, so-called peripheral fatigue. According to this theory, either the excessive accumulation or depletion of key chemicals interferes with cross bridge cycling in the exercising muscles impairing their capacity to produce force. This model has been called “catastrophic” [1] since it predicts that exercise is not regulated by the normal neuro-humoral controls active at rest and the function of which are to maintain homeostasis in all biological systems. According to this interpretation, physical activity represents a special biological case in which the need to maximize physical performance overrides the more conservative biological requirement to maintain homeostasis. Accordingly, this model predicts that exercise behaviours can be tolerated even if they lead to a catastrophic biological failure.

A variant of this model, so called central fatigue, proposes that related chemical changes in the brain alter cerebral function reducing the ability to maintain central motor drive to the exercising muscles.[2, 3] This model is also catastrophic since the cerebral changes are considered to be an inevitable consequence of the exercise behaviour and are therefore neither foreseeable, controllable, nor preventable.

An opposing model [4] holds that exercise performance is regulated by the central nervous system (CNS) to ensure that homeostasis is maintained, both at rest and during exercise, in all bodily systems, specifically to preclude any catastrophic biological failure. This model predicts that the brain regulates the behavior, specifically the exercise intensity, by continuously modifying the number of motor units that are recruited in the exercising muscles.[4] Recently we [5, 6] and others [7] have shown that the rating of perceived exertion (RPE), a marker of “fatigue”, rises as a linear function of the duration of exercise that remains. Furthermore, regardless of its intensity or duration, the exercise bout always terminates (i) at approximately the same (sub)maximal RPE levels and (ii) before there is evidence for any failure of whole body or local homeostasis.[8, 9] Since the rise in RPE is linear from the start of exercise, it suggests that the duration of the exercise bout is set early in exercise in an anticipatory manner. This has been termed “teleoanticipation”.[10]

An important prediction of this model is that all exercise performances are submaximal [1] since they terminate before there is a catastrophic metabolic or cardiorespiratory failure. This occurs because there is always a less-than-maximal recruitment of motor units in the exercising limbs.[11] The model also predicts that agents which interfere with these central regulatory controls in the central nervous system (CNS) could enhance exercise performance by allowing the body to approach more nearly its metabolic and cardio-respiratory limits.

It has been known for more than 60 years that certain drugs like the amphetamines that act principally in the brain, reduce fatigue at rest and enhance exercise performance.[12] Amphetamines markedly increase time to exhaustion during treadmill running [13] and cycling [14], increase running performance over distances of 600 yards to 1 mile by ~1.5% and weight lifting performance by 3-4%.[15] Amphetamines also attenuate fatigue during repetitive cycling sprints by approximately 30%.[16]

Surprisingly, few studies have investigated the mechanism by which centrally-acting drugs improve athletic performance but some suggest that they alter brain dopamine/serotonin ratios.[2, 3, 17]

To confirm that amphetamines do indeed improve exercise performance and to establish whether this effect is due either to a diminution of "peripheral fatigue" or to a central action in the brain, we used the rating of perceived exertion (RPE) to regulate the exercise behavior during submaximal exercise. This protocol allows subjects voluntarily to vary their work rates whilst maintaining a constant perception of effort. We have previously used this model to show the presence of a complex, intelligent regulatory system during exercise in the heat.[18] We have shown that rather than acting solely as a measure of exercise intensity, the conscious perception of effort plays a regulatory function to ensure that the work rate remains at an intensity that can be safely sustained for the expected duration of the exercise bout.[1] This is in contrast to a recently proposed model which proposes that feedback from fatiguing muscle plays an important role in the determination of central motor drive and force output, so that the development of peripheral muscle fatigue is confined to a certain level. In this model, the brain is regulated subconsciously and independent of perceived exertion.[19, 20]

We hypothesized that self-selected power output would decrease at a slower rate after the ingestion of methylphenidate and that the metabolic and cardio-respiratory stress would increase. This would indicate that subjects terminated the placebo trial with cardio-respiratory and metabolic reserve indicating that prolonged exercise performance is regulated by the central nervous system (CNS).

METHODS

Subjects

Eight elite cyclists (age 26.1 ± 5.3 yrs, height 181.0 ± 7.1cm, body mass 71.6 ± 8.1 kg, peak power output 437 ± 38 W, VO_{2Peak} 70.6 ± 6.8 $ml.kg^{-1}.min^{-1}$) were recruited for this study. Prior to participation in the study, the subjects were informed of the risks associated with the study. Informed consent was obtained in writing prior to the initiation of the study. All procedures conformed with the declaration of Helsinki.[21] The Research and Ethics Committee of the Faculty of Health Sciences of the University of Cape Town Medical School approved the study.

Testing Procedure

Subjects reported to the laboratory on four occasions. During the first two visits, subjects underwent anthropometric measurements, familiarization trials and preliminary testing for measurement of VO_{2Peak}. The subject's height (cm) and body mass (kg) were measured using a precision stadiometer and balance (Model 770, Seca, Bonn, Germany, accurate to 10g). Percentage body fat was calculated according to the equation of Durnin and Wormersley from skinfold measurements taken at seven sites.[22] During the third and fourth laboratory visits (experimental trials), subjects performed two cycling trials in random order, after ingestion of either 10mg methylphenidate or a placebo. In addition to power output, heart rate and EMG measurements, arterial blood was drawn from the radial artery (blood trials (n=4)) or respiratory gasses were collected (respiratory trials (n=4)) for measurement at 10min intervals. Subjects were asked to refrain from eating or drinking for at least 6 hours prior

to each of the performance tests. One and a half hours prior to each test, subjects were asked to randomly ingest either 10mg of methylphenidate or placebo prior to consuming a standardized meal comprising a 150g bran muffin and 250ml of orange juice. Each subject was asked to refrain from training for 24 hours prior to the VO_{2peak} test and to perform a 90 minute low intensity "recovery ride" 24 hours prior to the two experimental trials. They were also asked to refrain from consuming any caffeine or other stimulants on the day of each performance test. Prior to each testing session subjects were questioned to confirm that they had adhered to these instructions.

Preliminary testing

Tests were performed using either a Kingcycle or Computrainer Ergometer. Four subjects were tested using the Kingcycle ergometer. Due to the availability of the Computrainer ergometer, the remaining four subjects were tested using this device due to its greater capture rate, accuracy and reliability.[23] Each device was calibrated according to the manufacturer's guidelines prior to each testing session. Subjects completed a self-paced warm up for 15 minutes prior to each testing session. During both the progressive exercise test and the familiarization trials, the subjects were familiarized with the Borg RPE scale and a standard set of instructions was given for the subsequent trials.

Progressive exercise test

Testing for peak oxygen consumption (VO_{2peak}) was performed at a starting work rate of 2.50 W/kg body mass. The load was increased incrementally at a rate of 20 W every 60 seconds until the subject could not sustain a cadence greater than 70. During the progressive exercise test, ventilation volume (V_E), oxygen uptake (VO_2) and CO_2 production (VCO_2) were averaged over 15 second intervals using an on-line breath-by-breath gas analyser and pneumotach (Oxycon, Viasis, Hoechberg, Germany). Calibration of this device was performed prior to testing according to the manufacturer's instructions. VO_{2peak} was recorded as the highest VO_2 reading recorded for 30 seconds during the test. Peak power output (PPO) was calculated by averaging the power output for the final minute of the VO_{2peak} test. Subjects were requested to refrain from standing on the pedals throughout the test.

Familiarization trial

Within a week of performing the VO_{2peak} test, subjects reported to the laboratory for a familiarization session, during which they underwent procedures identical to the experimental trials. Subjects completed a cycling trial at a fixed RPE under the same conditions and procedures as the experimental trials (described below).

Cycle trials at a fixed rating of perceived exertion (RPE)

During experimental trials, subjects cycled at a fixed rating of perceived exertion (RPE). Subjects were instructed to cycle from the outset at a power output which they perceived represented an RPE of 16 on the Borg 6 to 20 Rating of Perceived Exertion scale.[24] This rating corresponded to the verbal cue of between "hard" and "very hard" on the Borg scale. The power output measured during the first three minutes of the trial was averaged to calculate an initial value. The trial was terminated when the power output fell below 70% of the initial value for two consecutive minutes. No feedback in terms of

distance covered, time elapsed, power output or heart rate was provided to the subject at any time during any trial. Subjects were allowed to ingest water ad libitum during the trials.

EMG testing

Prior to each experimental session, subjects performed three MVCs for normalization of the EMG signal which was obtained from the vastus lateralis muscle during the subsequent cycling bouts. We have previously used this method for normalization of the EMG signal obtained during sub-maximal [6, 18] cycling exercise. EMG activity was recorded from the right vastus lateralis muscle after attachment of a triode electrode (Thought Technology, West Chazy, N.Y., USA) was placed over the muscle belly and connected to a pre-amplifier. Outputs from the preamplifier were relayed to a Flexcomp/DSP EMG apparatus (Thought Technology USA) via a fiber optic cable and stored by an online computer. EMG signals were captured at 1984 Hz and analysed for five-second periods during the MVC and for five second periods at each measurement period during the trials. EMG data were analysed according to previously described methods.[18, 25] All processed iEMG data were normalized by dividing the iEMG obtained at each workload during the trials by the iEMG obtained during the MVC performed before the start of the trial. EMG data are therefore expressed as a percentage of the iEMG measured during the MVC. We have previously shown that this method of EMG normalization is reliable and valid for use in cycling trials.[18, 25]

Arterial Blood Samples

The subject's left or right radial artery was cannulated and connected to a three-way tap and thin extension tubing containing diluted heparin (10iu/ml).

Twenty ml of arterial blood was drawn prior to the start of trials and at 10 minute intervals during each trial for measurement of blood glucose, lactate, PO_2, PCO_2 and pH.

Respiratory Gas samples

Prior to the start and at 10 minute intervals during each trial, ventilation volume (V_E), oxygen uptake (VO_2) and CO_2 production (VCO_2) were measured over 45 second intervals using an on-line breath-by-breath gas analyser and pneumotach (Oxycon, Viasys, Hoechberg, Germany) as described for the progressive exercise test.

Additional Measurements

Heart rates were measured at the start of the trial and at 15 second intervals throughout the duration of the trial, using a Polar S720i heart rate monitor (Polar Electro OY, Kempele, Finland).

Power output readings were recorded at 30 second intervals by the Kingcycle ergometer and at 1 second intervals by the Computrainer ergometer. Power outputs were averaged for each 1 minute epoch prior to analysis.

Rating of perceived exertion was recorded every two-minutes. As required by the RPE clamp, subjects were required to ride constantly at an RPE of 16 using the Borg 6 to 20 rating of perceived exertion scale.[24]

Statistical Analysis

All statistical analyses were performed using STATISTICA version 7.0 (Stat-soft Inc., Tulsa, OK, USA). Power output, physiological variables and iEMG were analyzed using repeated measures ANOVA. Where a significant difference was found for either main effect (trial or time), a Tukey Post Hoc analysis was performed. Physiological variables were plotted against % of peak power values for each subject using GRAPHPAD PRISM version 3.0 (Graphpad Software Inc., San Diego, CA, USA). The slope and intercept values of the regression lines for each physiological variable were compared using a repeated measures ANOVA. Statistical significance was accepted when $P < 0.05$. A significant interaction was interpreted as meaning that the trials responded differently over time for that variable. All data are expressed as means ± standard deviation *(X ± s)*.

RESULTS

Exercise Performance

Initial power outputs (305 ± 33 vs 303 ± 46 W; NS; methylphenidate vs placebo) were the same in both trials. Power output fell significantly more slowly in the methylphenidate compared to the placebo trial (1.02 ± 0.28 vs 1.31 ± 0.42 W/min; $p<0.05$) (Fig. 1). As a result, total trial duration (terminated when power output fell below 70% of the starting value for more than 2 minutes) was significantly longer in the methylphenidate compared to the placebo trial (88.0 ± 23.1 vs 68.3 ± 16.9 minutes; $p<0.004$).

Furthermore, the power output was significantly higher in the methylphenidate trial at the equivalent time (68.3 ± 16.9 min) at which the subject terminated in the placebo trial (251 ± 33 W vs 211 ± 31 W; $p<0.0005$)(Table 1).

Table 1. Values for physiological variables measured at the point of fatigue (68 ± 18 min) during the placebo trial and at the equivalent time in the methylphenidate group.

Physiological Variable	Placebo	Methylphenidate	Difference (%)
Power (W)	210.6 ± 30.6	251.0 ± 33.1*	19
Heart Rate (bpm)	148.0 ± 10.3	165.3 ± 10.7*	12
#VO_2 (ml/min)	3428.3 ± 500.3	3864.8 ± 610.4*	13
#Ventilatory volume (l/min)	83.3 ± 22.4	92.9 ± 22.8*	11
#Arterial [lactate] (mmol/l)	1.2 ± 0.7	1.7 ± 1.0*	43

Values are means ± SD. * $P < 0.05$ for differences between trials. # n=4

Physiological variables

Heart rate

Mean heart rates were significantly higher in the methylphenidate than in the placebo trial (167 ± 7 vs 158 ± 10 beats/min; $p<0.01$)(Fig. 2A). Expressed relative to trial duration, heart rate decreased significantly in both trials ($p<0.01$)(Fig. 2A).

Heart rates were significantly higher in the methylphenidate trial at the equivalent time at which subjects terminated the placebo trial. (165 ± 11 vs 148 ± 10 bpm; $p<0.005$)(Table 1).

Oxygen consumption, Ventilatory volume and Cycling economy

Oxygen consumption (VO_2) was significantly higher in the methylphenidate trial at the equivalent time at which subjects terminated the placebo trial (3865 ± 610 vs 3428 ± 500 ml/min; $p<0.05$)(Table 1).

Ventilatory volumes (V'E) were significantly higher in the methylphenidate trial at the equivalent time at which subjects terminated the placebo trial (93 ± 23 vs 83 ± 22 l/min; $p<0.05$)(Table 1).

Mean values for cycling economy did not differ between the trials (14.4 ± 0.9 vs 14.1 ± 0.6 ml/W; methylphenidate vs placebo). The relationship between VO_2 and power output was not significantly different between groups (Fig. 3A), indicating that cycling economy was not altered by methylphenidate.

Arterial blood lactate concentrations

Arterial blood lactate concentrations did not differ significantly between the trials. When expressed as a percentage of completed distance ,lactate concentrations fell significantly over time in both trials ($p<0.0001$) (Fig. 2B), reaching the lowest levels at exercise termination. Methylphenidate did not alter the relationship between arterial lactate concentration and % PPO (Fig. 3B).

Arterial lactate concentrations were significantly higher in the methylphenidate trial at the equivalent time at which subjects terminated the placebo trial (1.75 ± 1.06 vs 1.23 ± 0.74 mmol/l; $p<0.05$) (Table 1).

Arterial blood glucose concentrations

Arterial blood glucose concentrations did not differ significantly between trials. A significant time effect was observed ($p<0.01$). Arterial glucose values initially increased until ~ 40% of trial duration and subsequently decreased (Fig. 2C).

Substrate utilization

Starting values for respiratory exchange ratios (RER) were the same but fell significantly ($p<0.0001$) with time in both trials (Fig. 2D). RER values were significantly lower for the final 20% of the methylphenidate than for the placebo trial ($p<0.05$) (Fig. 2D).

Arterial PO_2, PCO_2 and pH

The plots of arterial pH (Fig. 3C), PO_2 (Fig. 3D) and PCO_2 (Fig. 3E) against % PPO were not significantly different between trials.

iEMG activity

iEMG amplitude, expressed as a percentage of MVC, was not different at the start of the trials and fell significantly ($p<0.001$) with exercise duration (Fig. 2E). Although there were no differences in iEMG values between trials at the time at which subjects terminated the placebo trial, at 100% of trial duration iEMG amplitude was lower in the methylphenidate than in the placebo trial ($p<0.01$) (Fig. 2E).

DISCUSSION

Our first important finding was that methylphenidate slowed the rate at which power output fell when exercising at a fixed RPE (Fig. 1). As a result power output was approximately 19% higher and exercise duration 32% longer in the methylphenidate than in the placebo trial. This occurred even though, by design, subjects perceived both exercise bouts to be equally demanding (Table 1).

Secondly, this ergogenic effect of methylphenidate was not due to any reduction in metabolic or cardio-respiratory stress during exercise. Instead VO_2 (13%), heart rates (12%), ventilatory rates (11%), and arterial lactate concentrations (43%) were all significantly higher during the methylphenidate trial although arterial PO_2, PCO_2 and pH were not altered (Table 1).

Hence methylphenidate allowed subjects to sustain higher work rates and greater levels of metabolic and cardio-respiratory stress for longer, while perceiving the exercise stress to be identical. This indicates that subjects terminated the placebo trial with a metabolic and cardio-respiratory reserve that was not accessible without the use of methylphenidate. Methylphenidate allowed subjects to utilize this reserve presumably by removing the restraining effects of a CNS regulator [1] as first proposed by Lehman et al seventy years ago.[26] This finding proves that amphetamines do not enhance performance simply by preventing “peripheral fatigue” but is explained by a model of exercise [1, 4] in which there is metabolic and cardio-respiratory reserve to insure that whole body homeostasis is always preserved.[27]

The more popular theory that peripheral fatigue causes a progressive mechanical failure [28-30] predicts that methylphenidate could improve exercise performance by increasing the heart rate [14, 31, 32] and hence the cardiac output. By increasing oxygen delivery to the active muscles, methylphenidate might reverse “anaerobic” conditions in the muscles, thereby allowing exercise to continue at a higher VO_2. Four important findings disprove this interpretation.

First, arterial lactate concentrations were increased, not decreased, in the methylphenidate trials (Table 1) suggesting that if lactate production was due to anerobiosis (a theory which has been disproved over time [33]), then methylphenidate increased, rather than reduced such anerobiosis. Furthermore arterial lactate concentrations fell exponentially with exercise duration (Fig. 2B), dissociating (falling) arterial lactate concentrations as a cause of the linear reduction in power output as exercise progressed.

Second, iEMG activity fell during both trials (Fig 2E) in keeping with our model which predicts that changes in power output during prolonged exercise are due principally to altered central motor output to the exercising limb. Thus this linear fall in power output was due to a progressive reduction in the number of motor units recruited in the exercising limbs, as predicted.[1, 4] In contrast, if the linear fall in power output had been due solely to "peripheral fatigue", then iEMG activity would have either increased or stayed the same. Accordingly this study proves that the reduction in power output during exercise was associated with reduced central motor command to the exercising limb to which any peripheral fatigue, secondary to noxious biochemical changes [30], may or may not have contributed.

Furthermore, the finding that the EMG activity was never >45% of that achieved during a maximum voluntary contraction (MVC) indicates the presence of substantial motor recruitment reserve in the exercising limbs. Indeed if peripheral fatigue was the sole cause of the impaired performance during prolonged exercise, the CNS should increase the number of motor units active in the exercising limb, thereby delaying the onset of exhaustion until 100% of available motor units were recruited. The finding that the CNS does not adopt this policy indicates that the maximization of human exercise performance, regardless of cost, is not its principle priority. Since the CNS chooses to reduce the number of motor units recruited at the same RPE during prolonged exercise, its principal priority must rather be the protection of skeletal muscle integrity and the prevention of a catastrophic mechanical failure.

Although iEMG activity was not significantly different at the time at which subjects terminated the placebo trial, iEMG was not increased in the methylphenidate trial even though the power output was increased. Similarly iEMG and RER values recorded during the final 10% of the methylphenidate trials were significantly lower than those recorded at similar power outputs during the placebo trials. These values occurred at time points which exceeded the duration of the Placebo trials. There are a number of possible explanations for this unexpected finding.

Either (i) muscle contractility is increased by methylphenidate or (ii) these differences may be related to altered muscle recruitment patterns, for example a change from predominantly type II to type I muscle fiber recruitment secondary to glycogen depletion.[34-38] Or (iii) since a number of the methylphenidate trials exceeded 90 minutes in duration, there may have been an alteration in whole muscle recruitment patterns in these very prolonged trials.[39, 40] Although we did not measure this, (iv) increases in muscle temperature induced by altered thermoregulatory control in the methylphenidate trials may also have reduced iEMG amplitude during the later stages of these trials.[41, 42] Furthermore, (v) the greater duration of the methylphenidate trials may have affected iEMG amplitude due to increased sweat accumulation, electrode detachment or other factors affecting EMG signal strength.[43] Finally, the absolute difference between the control group and methylphenidate group of ~40W may have been insufficient to measure differences in muscle recruitment between groups. In previous studies a difference of <50W has not been associated with statistically significant differences in iEMG amplitude.[18, 44]

Our third relevant finding was that methylphenidate did not improve exercise performance either by altering cycling economy (VO_2 / power relationship (Fig. 3A) was not altered), or by improving respiratory efficiency or gaseous exchange (blood gas

measurements and the rate of ventilation were unchanged (Fig. 3C,3D,3E), or by altering metabolic substrate utilization as the RER was the same in both trials (Fig. 2D)

Fourth, we found that the initial power outputs were not different between trials (Table 1) (Fig. 1). As the power output was selected on the basis of each subject's perception of effort, this finding indicates that amphetamines do not alter those feed-forward controls that determine the choice of power output at the onset of exercise. However, methylphenidate caused the power output to fall less rapidly, presumably because it altered the manner in which the central regulator interpreted the continual afferent feedback from the numerous homeostatic sensors in the body. This allowed a higher power output and greater metabolic and cardio-respiratory stress to be tolerated at the same RPE.

Interestingly, amphetamines appear to have a greater ergogenic effect during prolonged submaximal exercise [13, 14] than during either maximal or short duration exercise.[15, 31] This suggests that amphetamines may influence selectively the central interpretation of afferent sensory feedback from some, but not all homeostatic regulators. Afferent sensory feedback related to thermoregulation appears particularly sensitive to this effect. Amphetamines improved performance during maximal 20km cycling time trials in hot environmental conditions [31] and a number of case reports describe the development of exertional heat stroke in athletes ingesting amphetamines.[45]

It might be argued that subjects do not normally exercise at a fixed RPE; rather the RPE typically rises as a function of the exercise duration that remains [5] whilst the work rate tends to show a bi-phasic pattern in which, following a fall, there is an increase near the end of exercise – the "end spurt". However, we controlled RPE as we have previously shown that the RPE is directly involved in the regulation of exercise performance.[6, 18] Thus we chose to investigate the effects of methylphenidate on power output independent of any effect on RPE.

Finally, we acknowledge that in high intensity exercise of short duration (< 2min) there may be a significant contribution of peripheral regulation to the impairment of exercise performance.[46]

SUMMARY AND CONCLUSIONS

In summary we confirm previous studies [12-16] showing that human exercise performance is substantially prolonged by a stimulant acting principally on the CNS. This proves that performance in the natural state can be substantially improved by chemical modulation of those unknown processes in the CNS that regulate exercise performance. The finding that humans exercise with a metabolic and cardio-respiratory reserve in the natural state indicates that the protection of homeostasis and the avoidance of mechanical failure in the exercising limbs is the more important consideration during exercise, as it is at rest.[1, 27] Hence human exercise performance is not normally regulated with the aim of achieving an ultimate athletic performance without any concern for the biological consequences.

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COMPETING INTERESTS

The authors declare that there are no competing interests.

FIGURES

Figure 1

Power expressed over 10 minute intervals.
Trial main effect, significantly different from placebo ($p<0.01$).
* Time main effect, decrease over time in both trials ($p<0.001$).

Figure 2

A: Heart rate expressed as a percentage of completed distance.
Significantly different from Methylphenidate ($p<0.01$).
* Time main effect, decrease over time in both trials ($p<0.01$).
B: Arterial blood lactate concentrations expressed as a percentage of completed distance.
* Time main effect, decrease over time in both trials ($p<0.0001$).
C: Arterial blood glucose concentrations expressed as a percentage of completed distance.
* Time main effect ($p<0.01$).
D: Respiratory exchange ratio (RER) expressed as a percentage of completed distance.
Significantly different from Placebo ($p<0.05$).
* Time main effect, decrease over time in both trials ($p<0.0001$).
E: iEMG activity expressed as a percentage of completed distance.
Significantly different from Placebo ($p<0.01$).
* Time main effect, decrease over time in both trials ($p<0.001$).

Figure 3

A: VO_2 expressed as a percentage of peak power for all trials.
B: Arterial blood lactate concentrations expressed as a percentage of peak power for all trials.
C: pH vs % peak power expressed as a percentage of peak power for all trials.
D: Arterial PO_2 vs % peak power expressed as a percentage of peak power for all trials.

E: PCO_2 vs % peak power expressed as a percentage of peak power for all trials.

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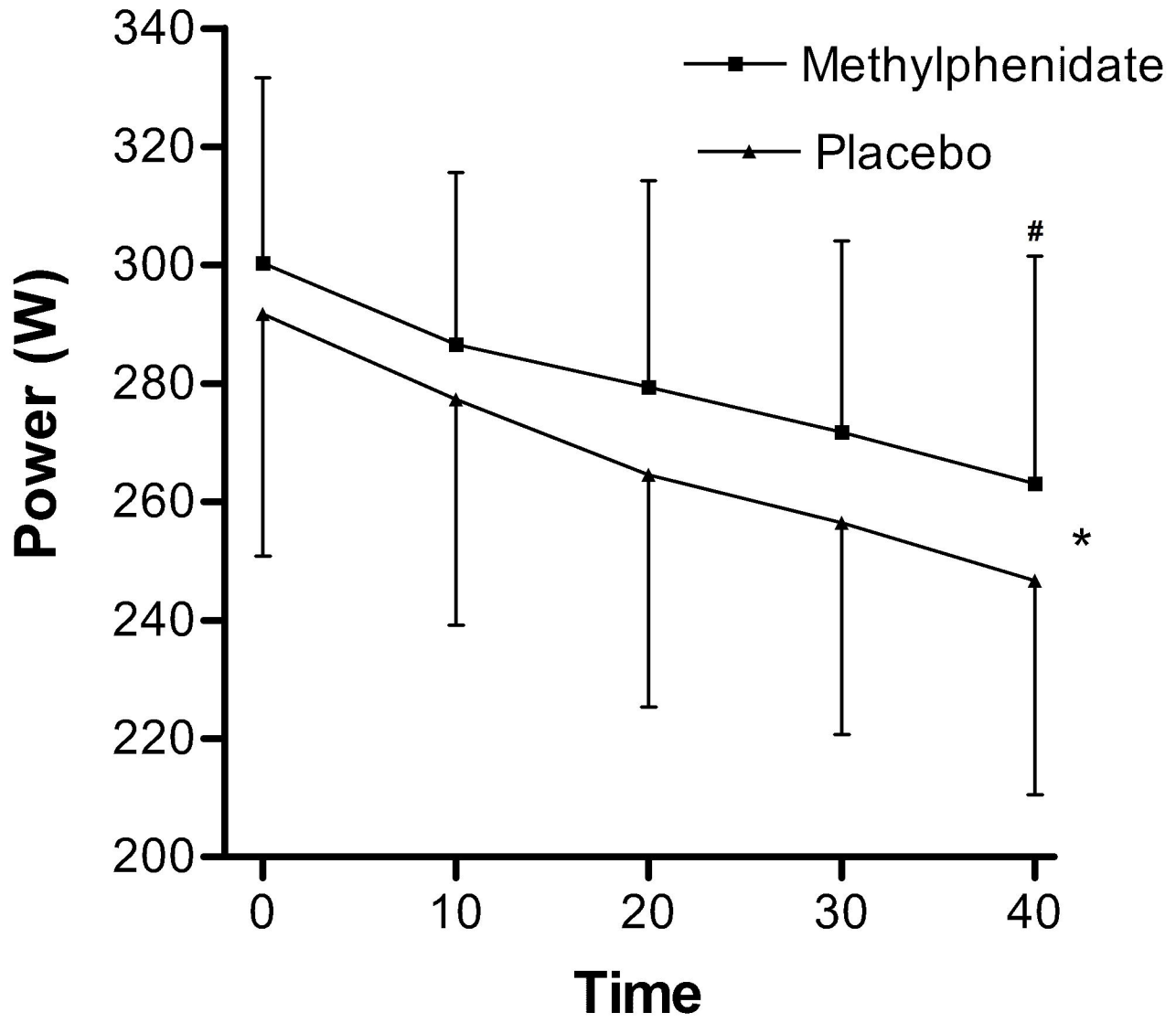
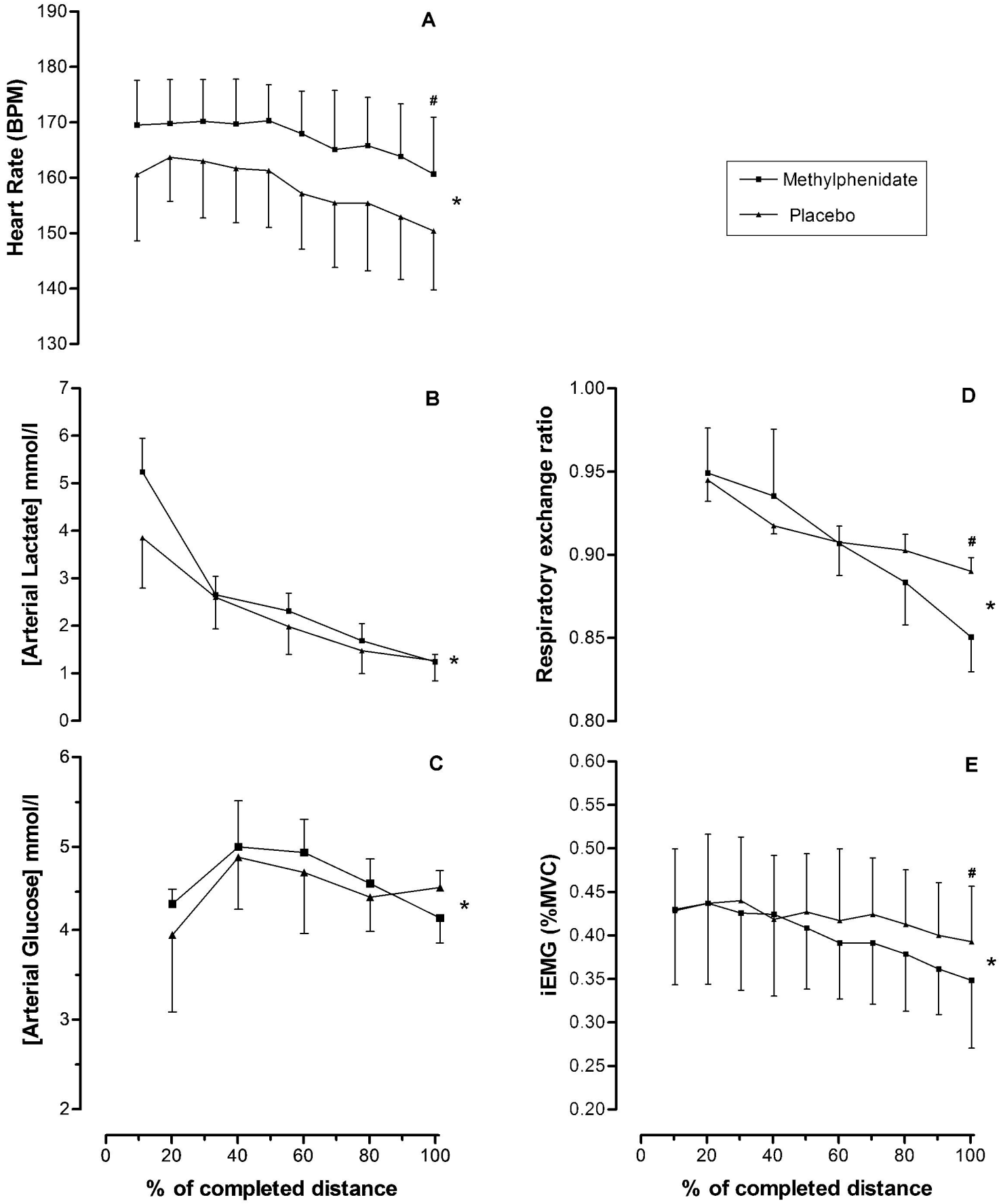

340
320
300
280
260
240
220
200
Power (W)
0
10
20
30
40
Time
Methylphenidate
Placebo
#
*


A
Heart Rate (BPM)
190
180
170
160
150
140
130
#
*
Methylphenidate
Placebo
B
[Arterial Lactate] mmol/l
7
6
5
4
3
2
1
0
*
D
Respiratory exchange ratio
1.00
0.95
0.90
0.85
0.80
#
*
C
[Arterial Glucose] mmol/l
6
5
4
3
2
*
E
iEMG (%MVC)
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
#
*
0
20
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60
80
100
% of completed distance
0
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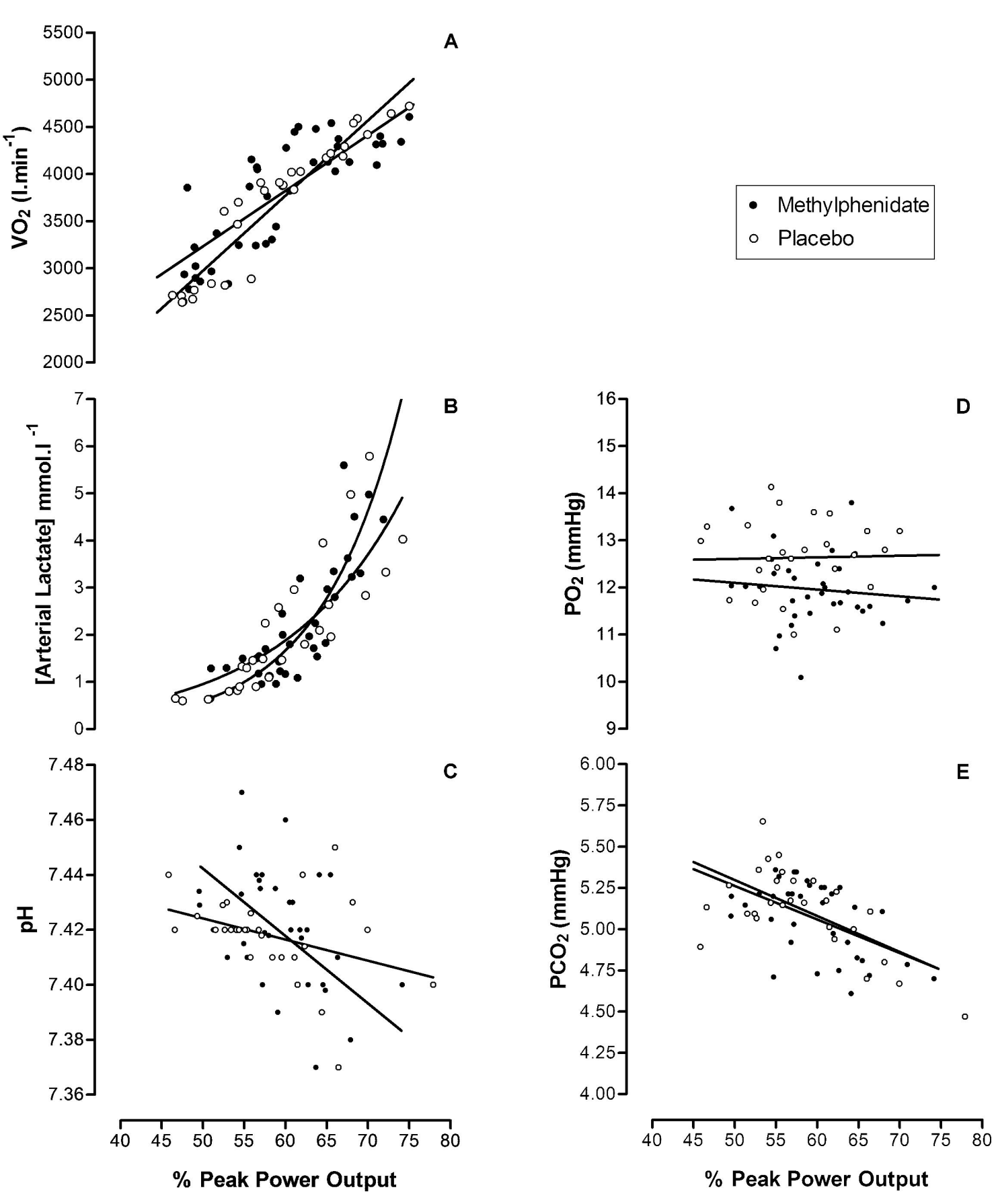
80
100
% of completed distance


A
B
C
D
E
VO_2 (l.min^{-1})
[Arterial Lactate] mmol.l^{-1}
pH
PO_2 (mmHg)
PCO_2 (mmHg)
% Peak Power Output
% Peak Power Output
Methylphenidate
Placebo

Exercising with reserve: Evidence that the CNS regulates prolonged exercise performance.

Jeroen Swart, Robert Patrick Lamberts, Michael Ian Lambert, Alan St Clair Gibson, Estelle Vicki Lambert, Justin Skowno and Timothy David Noakes

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