Northumbria Research Link

Citation: Elliott, Adrian, Skowno, Justin, Prabhu, Mahesh, Noakes, Timothy and Ansley, Les (2015) Evidence of cardiac functional reserve upon exhaustion during incremental exercise to determine VO2max. British Journal of Sports Medicine, 49 (2). pp. 128-132. ISSN 0306-3674

Published by: BMJ Publishing Group

URL: http://dx.doi.org/10.1136/bjsports-2012-091752 <http://dx.doi.org/10.1136/bjsports-2012-091752>

This version was downloaded from Northumbria Research Link: https://nrl.northumbria.ac.uk/id/eprint/11143/

Northumbria University has developed Northumbria Research Link (NRL) to enable users to access the University's research output. Copyright © and moral rights for items on NRL are retained by the individual author(s) and/or other copyright owners. Single copies of full items can be reproduced, displayed or performed, and given to third parties in any format or medium for personal research or study, educational, or not-for-profit purposes without prior permission or charge, provided the authors, title and full bibliographic details are given, as well as a hyperlink and/or URL to the original metadata page. The content must not be changed in any way. Full items must not be sold commercially in any format or medium without formal permission of the copyright holder. The full policy is available online: http://nrl.northumbria.ac.uk/policies.html

This document may differ from the final, published version of the research and has been made available online in accordance with publisher policies. To read and/or cite from the published version of the research, please visit the publisher's website (a subscription may be required.)

Northumbria University NEWCASTLE

University Library

Downloaded from bjsm.bmj.com on April 5, 2013 - Published by group.bmj.com
BJSM Online First, published on January 4, 2013 as 10.1136/bjsports-2012-091752

Evidence of cardiac functional reserve upon exhaustion during incremental exercise to determine VO_{2max}

Adrian D Elliott,[1,2] Justin Skowno,[3,4] Mahesh Prabhu,[5] Timothy David Noakes,[6] Les Ansley[7]

[1]School of Life Sciences, Kingston University, Surrey, UK
[2]Discipline of Physiology, University of Adelaide, Adelaide, Australia
[3]The Children's Hospital at Westmead, Sydney, Australiai
[4]Discipline of Paediatrics and Child Health, The University of Sydney, Sydney, Australia
[5]Freeman Hospital, Newcastle Upon Tyne, UK
[6]UCT/MRC Research Unit for Exercise Science and Sports Medicine, Department of Human Biology, University of Cape Town, Newlands, South Africa
[7]School of Psychology and Sports Sciences, Northumbria University, Newcastle Upon Tyne, UK

Correspondence to
Dr Adrian Elliott, School of Medical Sciences, University of Adelaide, Adelaide, 5062, Australia;
adrian.elliott@adelaide.edu.au

Received 6 September 2012
Revised 15 November 2012
Accepted 21 November 2012

ABSTRACT

Background There remains considerable debate regarding the limiting factor(s) for maximal oxygen uptake (VO_{2max}). Previous studies have shown that the central circulation may be the primary limiting factor for VO_{2max} and that cardiac work increases beyond VO_{2max}.

Aim We sought to evaluate whether the work of the heart limits VO_{2max} during upright incremental cycle exercise to exhaustion.

Methods Eight trained men completed two incremental exercise trials, each terminating with exercise at two different rates of work eliciting VO_{2max} (MAX and SUPRAMAX). During each exercise trial we continuously recorded cardiac output using pulse-contour analysis calibrated with a lithium dilution method. Intra-arterial pressure was recorded from the radial artery while pulmonary gas exchange was measured continuously for an assessment of oxygen uptake.

Results The workload during SUPRAMAX (mean±SD: 346.5±43.2 W) was 10% greater than that achieved during MAX (315±39.3 W). There was no significant difference between MAX and SUPRAMAX for Q (28.7 vs 29.4 L/min) or VO_2 (4.3 vs 4.3 L/min). Mean arterial pressure was significantly higher during SUPRAMAX, corresponding to a higher cardiac power output (8.1 vs 8.5 W; $p<0.06$).

Conclusions Despite similar VO_2 and Q, the greater cardiac work during SUPRAMAX supports the view that the heart is working submaximally at exhaustion during an incremental exercise test (MAX).

INTRODUCTION

Maximal oxygen uptake (VO_{2max}) is arguably the most researched parameter in exercise physiology. Its relationship with performance has been recognised since the pioneering work of Hill and Lupton[1] who concluded that oxygen uptake (VO_2) reached a maximum level during peak physical work, since interpreted as a plateau in the VO_2 response. Significant debate has surrounded the plateau phenomenon[2] although the concept of a truly maximal VO_2, established by supramaximal testing to verify that obtained from incremental exercise, is generally accepted.[3–5] However, there remains considerable debate regarding the factor(s) limiting VO_{2max}.[6–9] Broadly, the most commonly suggested mechanisms are that either a circulatory (cardiac) limitation or a neural (central) regulation determines the VO_{2max}.

It is established that skeletal muscle perfusion capacity exceeds the pumping capacity of the heart.[10 11] Secher *et al*[12] showed a reduction in leg blood flow when arm exercise is superimposed on maximal two-leg exercise, supporting the theory that the capacity to supply O_2 during maximal exercise is limited thereby constraining oxidative metabolism and, consequently, exercise capacity. Recently, a plateau in cardiac output (Q) close to exhaustion during both incremental and constant load maximal exercise[13 14] has been demonstrated. This has been interpreted as further evidence that the circulation limits VO_{2max}.

Opponents to the cardiac limitation theory propose that skeletal muscle recruitment is regulated through a central, neurally mediated mechanism during exhaustive exercise.[8 15–18] Proponents of this theory argue that this ensures myocardial ischaemia is avoided by moderating the demand placed on the heart, thereby preventing the attainment of an absolute maximum. This theory is supported by the findings that, in trained athletes, Q continues to increase linearly up until exhaustion without a plateau.[19–21]

Cardiac power output (CPO) is a measurement of cardiac function that incorporates both flow and pressure domains of the cardiovascular system and is measured as the product of Q and mean arterial pressure.[22] By measurement of CPO during maximal and supramaximal exercise, it becomes feasible to study the heart's ability to maintain circulation in the presence of increasing arterial pressure. During exercise at VO_{2max}, the measurement of CPO allows the exercise physiologist to determine whether the work of the heart continues to increase at the exercise intensity resulting in exhaustion. Should an increase in CPO be observed during exercise above that achieved at VO_{2max}, one might make one of two conclusions; that the heart is working submaximally during exercise at VO_{2max}[8] or, alternatively, that the circulation is absolutely maximal during exercise at VO_{2max} despite an increase in cardiac work.[23]

To differentiate between the theories explaining the limitation to maximal exercise, Brink-Elfegoun *et al*[23] designed an experiment in which two levels (100% and 110% VO_{2max}) of whole-body exercise were performed. VO_2 and Q were similar between workloads but blood pressure was significantly higher during exercise at 110% VO_{2max}, resulting in increased cardiac work.[22] The authors concluded that the greater cardiac *work* during supramaximal exercise indicates the absence of a central 'governor'. This conclusion was questioned by Noakes and Marino[8] who argued that these findings show the heart to be working submaximally at VO_{2max} and that the higher work rate achieved during a supramaximal bout indicates dissociation between Q and work rate, disproving the theory that Q regulates peak work rate and, consequently, VO_{2max}.

To cite: Elliott AD, Skowno J, Prabhu M, *et al*. *Br J Sports Med* Published Online First: [*please include* Day Month Year] doi:10.1136/bjsports-2012-091752

Copyright Article author (or their employer) 2013. Produced by BMJ Publishing Group Ltd under licence.

Downloaded from bjsm.bmj.com on April 5, 2013 - Published by group.bmj.com

Despite the extensive discussion on cardiac function and limitations during maximal exercise, CPO has not been measured continuously during maximal and supramaximal exercise, even in studies in which a plateau in VO_2[3] and Q[13 14] have been observed. The aims of this study were to evaluate the work of the heart during cycling exercise at maximal and supramaximal workloads. We hypothesised that the greater exercise workload would induce a greater circulatory and myocardial work demand, thus showing that the heart works submaximally at VO_{2max}, confirming the finding of Brink-Elfegoun *et al*.[23]

MATERIALS AND METHODS

Subjects

Eight recreationally trained male cyclists, age 40.5±9.2 years, body mass 80.5±10.9 kg, height 178.8±4.7 cm, VO_{2max} 53.7±6.5 ml/kg//min, volunteered to participate in the study. All participants were training for >5 h/week. Exclusion criteria for participation included a history of cardiopulmonary disease, lithium allergy and current therapy with lithium or muscle relaxants. The protocol was explained to the participants before they gave written informed consent. The research ethics committees at Northumbria University and Kingston University approved the study. All procedures were performed in accordance with national[24] and international (Declaration of Helsinki, 1964) guidelines.

Exercise protocol

Participants reported to the laboratory on a single occasion after abstaining from caffeine, alcohol and heavy exercise in the preceding 24 h. Participants performed two exercise trials during their visit, each separated by 1 h. Each trial, consisting of exercise conducted on an electromagnetically braked cycle ergometer (Velotron, Racermate Inc, Seattle, WA, USA), took place within an air-conditioned laboratory controlled to 22–23°C. The cycle ergometer was set up to each participant's specifications. Participants were allowed to self-select their cadence while remaining seated throughout each trial. The investigators provided consistent verbal encouragement throughout.

The first exercise trial (T1) consisted of an incremental protocol to exhaustion starting with 6 min at a power output of 120 W, increasing by 30 W every 3 min until the participant reached volitional exhaustion (MAX). Ventilatory threshold (VT) was determined according to the method of Beaver *et al*;[25] the workload for the second trial (T2) was derived from VT. During T2, participants each completed four exercise stages, each being separated by a 2 min recovery period at 100W. The first three stages consisted of 6 min at 120 W followed by 8 min each at 80% of VT, and 30% of the difference between power at VT and power at MAX. The final stage was performed at a power output 10% greater than that achieved during T1, until volitional fatigue (SUPRAMAX). The structure of T2 was designed so that the total exercise time was approximately similar to T1.

Measurements

Throughout each trial, pulmonary gas exchange was recorded continuously with an online gas analyser (Oxycon Pro, Jaeger, Germany). Participants wore a close-fitting facemask connected to a tripe-V sensor (Jaeger, Germany) consisting of a flow turbine and gas sampling tube. Prior to each trial, the gas analyser was calibrated using gas of a known composition (16% O_2; 4% CO_2; balance nitrogen). Volume calibration of the flow turbine was performed using a 3 l syringe over a range of flow rates.

Q was assessed continuously throughout each exercise by pulse contour analysis calibrated by an incorporated lithium dilution method (LiDCO, Cambridge, UK). The LiDCO device permits continuous haemodynamic recording by analysis of the radial artery pressure waveform (PulseCO, Cambridge, UK), calibrated by lithium dilution (LiDCO). Lithium dilution shows good agreement with thermodilution,[26 27] while continuous measurements have reported clinically acceptable accuracy and precision in critically ill patients.[26 28 29] During exercise, the LiDCO device compares favourably with direct Fick measurements during constant load and incremental exercise[30] and performs well during high-intensity exercise in trained cyclists.[31]

Prior to T1, a 21-gauge cannula was placed into a peripheral vein mid-way between the wrist and elbow of the right arm. A 20-gauge arterial cannula was then placed into the radial artery of the left arm under local anaesthesia (2% Lidocaine) and connected to an intensive care unit monitor (Hewlett Packard, Palo Alto, CA, USA) via a disposable pressure transducer (Philips M1567A, Philips, Germany), zeroed to ambient pressure. The pressure monitor provides continuous arterial pressure waveform data to the LiDCO monitor. The LiDCO system calculates a nominal stroke volume from a pressure–volume transformation of the arterial pressure waveform, which is then converted to absolute stroke volume using the incorporated lithium dilution method.

Lithium dilution calibration involved the administration of a lithium chloride bolus (0.3–0.45 mM) into the peripheral vein. The bolus was immediately followed by a 20 ml saline flush. A lithium dilution curve was subsequently derived by drawing arterial blood past a lithium sensor connected to the arterial cannula, at a constant flow rate using a flow pump. Q was calculated according to the following equation:[32]

$$Q = [\text{LiCl dose (mM)} \times 60]/[\text{area under dilution curve (mM/L/s)} \times (1 - \text{PCV})]$$

where PCV=haemoglobin (g/dl)/33

Heart rate (HR) was calculated by the duration between subsequent pressure waveforms. Arterial pressure was recorded directly by the LiDCO monitor from the arterial pressure trace. LiDCO calibrations were performed during the SUPRAMAX workload of T2 and applied to all Q data. Calibration procedures began 1 min into the SUPRAMAX stage. The pulse contour analysis data required for calibration with the lithium dilution method was obtained by interpolation of the mean values in the 10 s preceding and succeeding the calibration period to ensure that all data were time-matched. This calibration factor was applied retrospectively to all data obtained during the study.

CPO and rate-pressure product (RPP) were calculated according to the following equations:[22]

$$\text{CPO(W)} = Q \times \text{MAP} \times k$$

where $k=2.22\times10^{-3}$ and MAP=mean arterial pressure (mm Hg).[33]

$$\text{RPP(beats/min} \times \text{mm Hg)} = \text{HR} \times \text{SBP}$$

where SBP=systolic blood pressure (mm Hg)

$$\text{MAP(mm Hg)} = \text{DBP} + 1/3(\text{SBP} - \text{DBP})$$

where DBP=diastolic blood pressure (mm Hg).

Downloaded from bjsm.bmj.com on April 5, 2013 - Published by group.bmj.com

Data analysis

Haemodynamic and pulmonary gas exchange data were averaged over 10 s epochs throughout both T1 and T2. Data for MAX and SUPRAMAX were taken at the time point of maximal Q. Data analysis was performed with GraphPad Prism V.5. A paired t test was performed to compare MAX and SUPRAMAX data. Statistical significance was determined at $p<0.05$. All data are presented as means±SD unless otherwise stated.

RESULTS

The workloads for MAX and SUPRAMAX were 315±39.3 W and 346.5±43.2 W, respectively. Time to exhaustion was not significantly different between MAX and SUPRAMAX trials (176±12.6 vs 170±40.7 s).

Peak exercise data are shown in table 1.There was no significant difference between MAX and SUPRAMAX (figure 1) for Q (28.7 vs 29.4 l/min, 95% CI −2.6 to 1.4; p=0.48), VO_2 (4.26 vs 4.26 l/min, 95% CI −0.18 to 0.17; p=0.96), stroke volume (154.1 vs 157.3 ml, 95% CI −13.5 to 7.1; p=0.49) or HR (188.9 vs 190.1 beats/min, 95% CI −4.3 to 1.8; p=0.36), respectively. MAP was significantly higher at peak exercise during the SUPRAMAX stage (129.1 vs 134.6 mm Hg, 95% CI −10.1 to −0.9; p=0.03), although both systolic and diastolic blood pressure remained unchanged between workloads. In addition, no significant differences were observed for Q, SV, HR, MAP or VO_2 between peak values and exhaustion during either exercise stage. Both Q (Q/W; 91.6±18.4 vs 85.3±21.4 ml/W; 95% CI 1.24 to 11.31; p=0.02) and VO_2 (VO_2/W; 13.5±1.1 vs 12.3±1.5 ml/W; 95% CI 0.71 to 1.69; p=0.0007) expressed per unit of power output, were significantly greater during the MAX stage.

The significantly greater MAP at the SUPRAMAX workload led to a tendency for a greater CPO (8.1 vs 8.5 W, 95% CI −0.92 to 0.02), although this did not reach statistical significance (p=0.06). RPP was not significantly different between MAX and SUPRAMAX (41, 625 vs 41, 546 beats/min/mm Hg, 95% CI −3222 to 3378; p=0.96).

DISCUSSION

The most significant finding from this study was that although Q was similar, the work performed by the heart, assessed by CPO, was increased during supramaximal exercise compared with maximal exercise due to higher mean arterial pressure. Although this did not reach statistical significance, the 95% CIs indicate a substantial increase that is likely to be of biological significance. This confirms previous findings[23] during combined arm and leg exercise. These findings indicate an increase in the work performed by the heart during supramaximal exercise with a greater myocardial VO_2.[22]

Table 1 Mean (SD) exercise data obtained from MAX and SUPORAMAX trials

Variable	MAX (n=8)	SUPRAMAX (n=8)
Power output (W)	315 (39.3)	346.5 (34.2)
Q (l/min)	28.7 (5.9)	29.4 (7.0)
VO_2 (l/min)	4.26 (0.61)	4.26 (0.7)
SV (ml)	154.1 (30.9)	157.3 (34.4)
HR (bpm)	189 (10)	190 (13)
MAP (mm Hg)	129 (11)	135 (12)
SBP (mm Hg)	222 (28)	224 (33)
DBP (mm Hg)	78 (6)	81 (8)
CPO (W)	8.05 (1.9)	8.5 (2.1)
RPP (beats/min/mm Hg)	41, 625 (4347)	41, 456 (5489)

CPO, cardiac power output; DBP, diastolic blood pressure; HR, heart rate; MAP, mean arterial pressure; RPP, rate-pressure product; SBP, systolic blood pressure; SV, stroke volume; Q, cardiac output; VO_2, oxygen uptake.

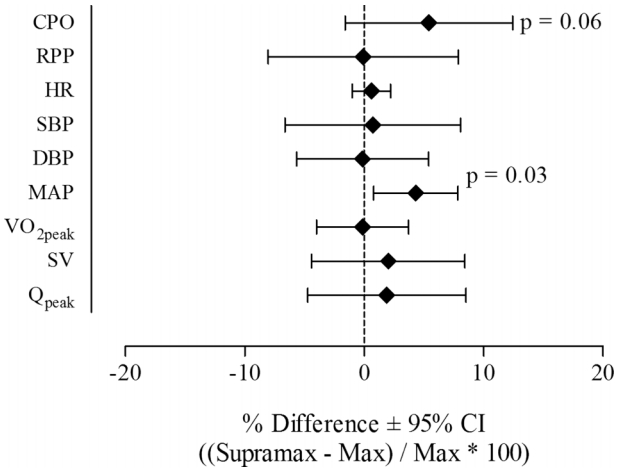

Figure 1 Forrest plot displaying mean percentage differences (±95% CI) of measurements between SUPRAMAX and MAX exercise. All data are time aligned to measurement of peak cardiac output.

The observation that, at maximal exercise, further elevations in workload occur without any additional increase in Q and VO_2 suggests that, in health, the attainment of VO_{2max} is accompanied by an attenuated increase in systemic blood flow, as frequently argued.[6 11 14 34–36] It is known that the maximally vasodilated skeletal muscle in humans can accept a greater blood flow than the heart can supply (ie, greater than Q_{max}).[10–12] Furthermore, a number of experimental manipulations of O_2 delivery have resulted in the reduction of VO_{2max},[35 37 38] supporting the theory that O_2 delivery constrains VO_{2max} during exercise. However, the findings that the heart is able to increase its work output beyond that achieved during VO_{2max} testing, as previously shown,[23] confirms that typical incremental exercise to VO_{2max}, as observed during the MAX trial, terminates with some degree of cardiac functional reserve.

Our findings of a similar VO_{2max} between MAX and SUPRAMAX support the concept of a true maximal VO_2 observed by a number of groups comparing maximal and supramaximal exercise [3–5] although alternative testing methods, such as a decremental test in which exercise intensity starts high and decreases, may yield higher VO_{2max} values.[39] By the same principle, the absence of any increase in Q despite a greater workload during SUPRAMAX indicates that a maximal Q is achieved at the termination of incremental and constant-load exhaustive exercise, although the Q response to alternative testing methods producing higher VO_{2max} have not been investigated. The observation that Q fails to increase at or near maximal exercise has been demonstrated previously. [13 14 23 36 40–42]

The theory of a central, neurally mediated limitation[15] predicts that the loss of homeostasis during exhaustive exercise is avoided by the actions of a centrally located 'governor' that limits skeletal muscle recruitment, thus reducing the likelihood of any homeostatic disturbances, including both metabolic and/or thermoregulatory regulation.[17] Our findings that circulation appears maximal during exercise to exhaustion do not exclude the existence of a governor within the central nervous system that anticipates significant homeostatic disturbance(s), therefore limiting any further increase in myocardial VO_2 and risking the

Downloaded from bjsm.bmj.com on April 5, 2013 - Published by group.bmj.com

onset of myocardial ischaemia. The observation that the heart appears to be work submaximally during exercise eliciting VO_{2max}[23] supports a central limitation theory by posing the question of why the heart does not work harder at VO_{2max} despite its apparent capacity to do so.[8] One interpretation is that a central regulator may limit myocardial oxygen demand by preventing additional skeletal muscle recruitment at the point of exhaustion during maximal exercise.

However, the greater workload during SUPRAMAX would require additional motor unit recruitment [43 44] that, in the view of the central limitation theory, should be regulated to constrain Q.[8] It has been argued that it remains unclear as to how a central 'governor' would terminate exercise at VO_{2max} when there is evidence that greater skeletal muscle recruitment[43] and workloads[5] are achievable in the absence of significant homeostatic disturbances or myocardial ischaemia. However, there are several points worth noting; First, the central theory proposes that exercise terminates *before* there is maximal skeletal muscle activation,[17] as shown elsewhere.[43 45] Second, a dissociation between Q and exercise power output appears during SUPRAMAX such that Q/W is significantly lower than that measured during MAX, suggestive of a an uncoupling between workload and cardiovascular function. This finding confirms that Q does not determine skeletal muscle work. Finally, one should consider how supramaximal exercise as a separate effort, as conducted here and elsewhere [3 5 23] influences this discussion. It is plausible that the degree of 'homeostatic disturbance' differs during a separate supramaximal bout. Indeed, Mortensen *et al*,[14] with a similar experimental model, observed greater disturbances to blood pH, lactate and body temperature during incremental exercise to VO_{2max} as compared with constant-load supramaximal exercise. One could postulate that supramaximal exercise performed separately provides no greater metabolic/homeostatic challenge than maximal exercise performed at the end of incremental exercise, with the consequence that constant-load supramaximal exercise requires little constraint from a central 'governor' in the initial stages.

While it is agreed that a maximal VO_2 exists, this study and others [39] suggest that neither Q nor VO_2 are maximal during incremental exercise to exhaustion. Despite efforts to portray the VO_{2max} measured during incremental exercise as being limited by the circulation,[44] the submaximal cardiac function observed during 'maximal' exercise in this study and others[23] suggests that this form of exercise testing may not be a useful evaluation of exercise performance[46] or for the evaluation of maximal cardiac function in healthy humans.

Direct Fick and/or thermodilution are typically considered 'gold standard' methods for Q measurement during exercise. However, the technical difficulties and risk[47] associated with these methodologies renders them unsuitable for most exercise studies. Furthermore, previous studies employing these methods, and others, are typically only able to assess Q at one or two timepoints during maximal exercise, thus potentially recording submaximal values. Our method of assessment provides continuous measurements throughout exercise up until exhaustion,[31] with only minimal risk and invasiveness. Therefore, we were able to be absolutely sure that we obtained a maximal measure for Q. Lithium dilution has proven accuracy in the clinical setting in critically ill patients[27 48 49] patients with hyperdynamic circulation[50] and exercising heart failure patients.[30] In this study, we were able to successfully calibrate the device during the SUPRAMAX exercise stage, with this calibration factor being applied to all exercise data. Importantly, we were also able to obtain true peak Q and arterial pressure measurements, regardless of the timepoint at which they occurred. We believe this provides significant benefit when assessing the haemodynamic response to maximal exercise, which is typically of short duration.

Our study is not without limitations. First, we chose to perform all testing in one session for practical reasons relating to the procedures associated with Q measurement. Likewise, we did not counterbalance the order of trials. This was to allow us to ensure that the SUPRAMAX exercise trial did not impact upon data obtained from a subsequent MAX trial. Both of these limitations mirror those relevant to the Brink-Elfegoun *et al*[23] study therefore permitting comparisons between the two studies. Additionally, we chose upright cycling as our testing modality. Incremental cycle exercise is the common modality of maximal exercise testing for the determination of VO_{2max} and has been shown to elicit a plateau in VO_2 suggestive of the true attainment of VO_{2max}. Future studies should attempt to determine the cardiovascular responses to exercise in trials where recent evidence has shown the potential for increased VO_2 during alternative protocols to those used in this study.[39] We also acknowledge the limitations of Q measurement. We chose a method that permitted continuous measurements of Q throughout maximal exercise and therefore measurements in the period immediately preceding exhaustion. Pulse-contour analysis with lithium dilution calibration has shown close agreement with gold standard methods during exercise.[30] Finally, this study's small sample size increased the chances of a type II error due to insufficient statistical power. Sample size was largely dictated by the requirement to perform invasive procedures of healthy participants during strenuous exercise. Future studies attempting to address this research question should consider a statistical power

What are the new findings

- This study shows that cardiac power output is submaximal during an incremental cycle exercise test to exhaustion.
- Using a novel approach to measuring cardiac output during exercise, both oxygen uptake and cardiac output do not increase with a subsequent supramaximal exercise bout.
- This study supports the theory of a central governor that constrains VO_{2max}, despite an apparent cardiovascular reserve upon exhaustion.

How might it impact on clinical practice in the near future

- The potential clinical relevance of this study is that a typical incremental exercise test to determine VO_{2max} may not provide an accurate reflection of full cardiac pumping capacity.
- Clinicians and/or exercise physiologists should consider the potential use of a supramaximal exercise protocol to establish a more accurate assessment of cardiac pumping capacity.
- Additionally, this study provides evidence of a practical, continuous method for the measurement of cardiac output during exercise testing.

Downloaded from bjsm.bmj.com on April 5, 2013 - Published by group.bmj.com

analysis to determine the required sample size to detect the differences observed during this study and others.

In conclusion, this study shows that during two levels of maximal cycling exercise, differing by a workload of 10% and eliciting identical VO_{2max}, cardiac work continues to increase despite Q remaining the same. These findings suggest that cycling exercise to VO_{2max} terminate with cardiac functional reserve, yet maximal Q.

Contributors All authors were involved with the planning and design of the study. AE, JS, MP and LA were responsible for data collection. All authors contributed to analysis and interpretation of the data. AE was responsible for the first draft of the manuscript, which was subsequently revised by all authors. All authors agreed the final version of the manuscript.

Funding None.

Competing interests None.

Ethics approval Kingston University and Northumbria University.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Hill AVE, Lupton H. Muscular exercise, lactic acid, and the supply and utilization of oxygen. *QJM* 1923;16:135–71.
2 Midgley AW, McNaughton LR, Polman R, *et al*. Criteria for determination of maximal oxygen uptake: a brief critique and recommendations for future research. *Sports Med* 2007;37:1019–28.
3 Rossiter HB, Kowalchuk JM, Whipp BJ. A test to establish maximum O_2 uptake despite no plateau in the O_2 uptake response to ramp incremental exercise. *J Appl Physiol* 2006;100:764–70.
4 Foster C, Kuffel E, Bradley N, *et al*. VO_{2max} during successive maximal efforts. *Eur J Appl Physiol* 2007;102:67–72.
5 Hawkins MN, Raven PB, Snell PG, *et al*. Maximal oxygen uptake as a parametric measure of cardiorespiratory capacity. *Med Sci Sports Exerc* 2007;39:103–7.
6 Saltin B, Calbet JA. Point: in health and in a normoxic environment, $VO_{2\ max}$ is limited primarily by cardiac output and locomotor muscle blood flow. *J Appl Physiol* 2006;100:744–5.
7 Wagner PD. Counterpoint: in health and in normoxic environment VO_{2max} is limited primarily by cardiac output and locomotor muscle blood flow. *J Appl Physiol* 2006;100:745–7; discussion 747–8.
8 Noakes TD, Marino FE. Point:counterpoint: maximal oxygen uptake is/is not limited by a central nervous system governor. *J Appl Physiol* 2009;106:338.
9 Gonzalez-Alonso J, Mortensen SP. Comments of point:counterpoint: maximal oxygen uptake is/is not limited by a central nervous system governor. *J Appl Physiol* 2009;106:344–5.
10 Andersen P, Saltin B. Maximal perfusion of skeletal muscle in man. *J Physiol* 1985;366:233.
11 Calbet JA, Rådegran G, Boushel R, *et al*. Plasma volume expansion does not increase maximal cardiac output or $VO_{2\ max}$ in lowlanders acclimatized to altitude. *Am J Physiol Heart Circ Physiol* 2004;287:H1214–24.
12 Secher NH, Clausen JP, Klausen K, *et al*. Central and regional circulatory effects of adding arm exercise to leg exercise. *Acta Physiol Scand* 1977;100:288–97.
13 Mortensen SP, Dawson EA, Yoshiga CC, *et al*. Limitations to systemic and locomotor limb muscle oxygen delivery and uptake during maximal exercise in humans. *J Physiol* 2005;566(Pt 1):273–85.
14 Mortensen SP, Damsgaard R, Dawson EA, *et al*. Restrictions in systemic and locomotor skeletal muscle perfusion, oxygen supply and VO_2 during high-intensity whole-body exercise in humans. *J Physiol* 2008;586:2621.
15 Noakes TD. 1996 J. B. Wolffe Memorial Lecture. Challenging beliefs: ex Africa semper aliquid novi. *Med Sci Sports Exerc* 1997;29:571–90.
16 Noakes TD. Physiological models to understand exercise fatigue and the adaptations that predict or enhance athletic performance. *Scand J Med Sci Sports* 2000;10:123–45.
17 Noakes TD, St Clair Gibson A. Logical limitations to the 'catastrophe' models of fatigue during exercise in humans. *Br J Sports Med* 2004;38:648–9.
18 Noakes TD. Fatigue is a brain-derived emotion that regulates the exercise behavior to ensure the protection of whole body homeostasis. *Front Physiol* 2012;382:1–13.
19 Gledhill N, Cox D, Jamnik R. Endurance athletes' stroke volume does not plateau: major advantage is diastolic function. *Med Sci Sports Exerc* 1994;26:1116.
20 Zhou B, Conlee RK, Jensen R, *et al*. Stroke volume does not plateau during graded exercise in elite male distance runners. *Med Sci Sports Exerc* 2001;33:1849.
21 Calbet JA, Gonzalez-Alonso J, Helge JW, *et al*. Cardiac output and leg and arm blood flow during incremental exercise to exhaustion on the cycle ergometer. *J Appl Physiol* 2007;103:969–78.
22 Cooke GA, Marshall P, al-Timman JK, *et al*. Physiological cardiac reserve: development of a non-invasive method and first estimates in man. *Heart* 1998;79:289–94.
23 Brink-Elfegoun T, Kaijser L, Gustafsson T, *et al*. Maximal oxygen uptake is not limited by a central nervous system governor. *J Appl Physiol* 2007;102:781–6.
24 Hull JH, Ansley P, Ansley L. Human Tissue Act: implications for sports science. *Br J Sports Med* 2008;42:236–7.
25 Beaver WL, Wasserman K, Whipp BJ. A new method for detecting anaerobic threshold by gas exchange. *J Appl Physiol* 1986;60:2020–7.
26 Kurita T, Morita K, Kato S, *et al*. Comparison of the accuracy of the lithium dilution technique with the thermodilution technique for measurement of cardiac output. *Br J Anaesth* 1997;79:770.
27 Linton R, Band D, O'Brien T, *et al*. Lithium dilution cardiac output measurement: a comparison with thermodilution. *Crit Care Med* 1997;25:1796–800.
28 Cecconi M, Dawson D, Casaretti R, *et al*. A prospective study of the accuracy and precision of continuous cardiac output monitoring devices as compared to intermittent thermodilution. *Minerva Anestesiol* 2010;76:1010–17.
29 Linton RA, Jonas MM, Tibby SM, *et al*. Cardiac output measured by lithium dilution and transpulmonary thermodilution in patients in a paediatric intensive care unit. *Intensive Care Med* 2000;26:1507–11.
30 Kemps HMC, Thijssen EJM, Schep G, *et al*. Evaluation of two methods for continuous cardiac output assessment during exercise in chronic heart failure patients. *J Appl Physiol* 2008;105:1822–9.
31 Elliott A, Skowno J, Prabhu M, *et al*. Measurement of cardiac output during exercise in healthy, trained humans using lithium dilution and pulse contour analysis. *Physiol Meas* 2012;33:1691–701.
32 Linton RA, Band DM, Haire KM. A new method of measuring cardiac output in man using lithium dilution. *Br J Anaesth* 1993;71:262–6.
33 Nelson RR, Gobel FL, Jorgensen CR, *et al*. Hemodynamic predictors of myocardial oxygen consumption during static and dynamic exercise. *Circulation* 1974;50:1179–89.
34 Mitchell JH, Sproule BJ, Chapman CB. The physiological meaning of the maximal oxygen intake test. *J Clin Invest* 1958;37:538–47.
35 Ekblom B, Huot R, Stein EM, *et al*. Effect of changes in arterial oxygen content on circulation and physical performance. *J Appl Physiol* 1975;39:71–5.
36 Gonzalez-Alonso J, Calbet JAL. Reductions in systemic and skeletal muscle blood flow and oxygen delivery limit maximal aerobic capacity in humans. *Circulation* 2003;107:824.
37 Koskolou MD, Roach RC, Calbet JA, *et al*. Cardiovascular responses to dynamic exercise with acute anemia in humans. *Am J Physiol* 1997;273(4 Pt 2):H1787–93.
38 Calbet JA, Boushel R, Rådegran G, *et al*. Determinants of maximal oxygen uptake in severe acute hypoxia. *Am J Physiol Regul Integr Comp Physiol* 2003;284: R291–303.
39 Beltrami FG, Froyd C, Mauger AR, *et al*. Conventional testing methods produce submaximal values of maximum oxygen consumption. *Br J Sports Med* 2012;46:23–9.
40 Stringer WW, Hansen JE, Wasserman K. Cardiac output estimated noninvasively from oxygen uptake during exercise. *J Appl Physiol* 1997;82:908–12.
41 González-Alonso J, Dalsgaard MK, Osada T, *et al*. Brain and central haemodynamics and oxygenation during maximal exercise in humans. *J Physiol* 2004;557(Pt 1):331–42.
42 Stringer WW, Whipp BJ, Wasserman K, *et al*. Non-linear cardiac output dynamics during ramp-incremental cycle ergometry. *Eur J Appl Physiol* 2005;93:634–9.
43 Brink-Elfegoun T, Holmberg HC, Ekblom MN, *et al*. Neuromuscular and circulatory adaptation during combined arm and leg exercise with different maximal work loads. *Eur J Appl Physiol* 2007;101:603–11.
44 Levine BD. VO_{2max}: what do we know, and what do we still need to know? *J Physiol* 2008;586:25–34.
45 Albertus Y. Critical analysis of techniques for normalising electromyographic data. PhD thesis, University of Cape Town, South Africa, 2008.
46 Noakes TD. Time to move beyond a brainless exercise physiology: the evidence for complex regulation of human exercise performance. *Appl Physiol Nutr Metab* 2011;36:23–35.
47 Scheer B, Perel A, Pfeiffer UJ. Clinical review: complications and risk factors of peripheral arterial catheters used for haemodynamic monitoring in anaesthesia and intensive care medicine. *Crit Care* 2002;6:199–204.
48 Hamilton TT, Huber LM, Jessen ME. PulseCO: a less-invasive method to monitor cardiac output from arterial pressure after cardiac surgery. *Ann Thorac Surg* 2002;74:S1408–12.
49 Pittman J, Bar-Yosef S, SumPing J, *et al*. Continuous cardiac output monitoring with pulse contour analysis: a comparison with lithium indicator dilution cardiac output measurement. *Crit Care Med* 2005;33:2015.
50 Costa MG, Della Rocca G, Chiarandini P, *et al*. Continuous and intermittent cardiac output measurement in hyperdynamic conditions: pulmonary artery catheter vs. lithium dilution technique. *Intensive Care Med* 2008;34:257–63.

Downloaded from bjsm.bmj.com on April 5, 2013 - Published by group.bmj.com

Evidence of cardiac functional reserve upon exhaustion during incremental exercise to determine VO_{2max}

Adrian D Elliott, Justin Skowno, Mahesh Prabhu, et al.

Br J Sports Med published online January 4, 2013
doi: 10.1136/bjsports-2012-091752

Updated information and services can be found at:
http://bjsm.bmj.com/content/early/2013/01/04/bjsports-2012-091752.full.html

These include:

References This article cites 48 articles, 25 of which can be accessed free at:
http://bjsm.bmj.com/content/early/2013/01/04/bjsports-2012-091752.full.html#ref-list-1

P<P Published online January 4, 2013 in advance of the print journal.

Email alerting service Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

Advance online articles have been peer reviewed, accepted for publication, edited and typeset, but have not not yet appeared in the paper journal. Advance online articles are citable and establish publication priority; they are indexed by PubMed from initial publication. Citations to Advance online articles must include the digital object identifier (DOIs) and date of initial publication.

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/