The effect of ischaemic preconditioning (IPC) on exercise performance is an increasingly popular topic in sports science. This article will present the key practical considerations for using IPC prior to sports performance, supported by discussion of both the current literature findings and potential mechanisms that may underpin changes in human performance.

THE SEARCH FOR ERGOGENIC STRATEGIES IN SPORT

Extremely fine margins exist in sport, with under one hundredth of a second historically being the difference between gold and silver medals in Olympic events such as swimming, rowing, 100 m and 400 m track (to name a few). Consequently, the competitive nature of elite sport in the present era pushes/encourages athletes and sports scientists to find novel strategies (where legally permitted) to maximise competitive performance. Periodised training programmes developed by coaches and scientists plan to ensure optimal performance occurs on competition day. Regardless of training preparation, certain pre-competition strategies exist, capable of further enhancing performance. The problem with some proven ergogenic aids is that they often carry complications or lack practicality in applied competitive settings (i.e. potential anti-doping violations or technological limitations). Ergogenic/preconditioning strategies come in many forms (nutritional supplementation, post-activation potentiation, prior high-intensity exercise priming and passive heating/cooling).

BACKGROUND OF IPC

IPC is a method whereby brief episodes of ischaemia (either 3 x 5 or 4 x 5 minutes of arterial blood flow occlusion interspersed with 5 minutes of reperfusion) are administered to a limb in order to increase a tissue's tolerance to prolonged ischaemic exposures. IPC represents a hormetic biphasic dose-response phenomenon and reduces tissue infarct size following both

THE STORY SO FAR

– Written by Scott Cocking, Qatar
IPC remains unproven and requires further investigation. Cuff placement Depending on exercise modality, the cuff can be placed locally (applied to the exercising limb) or remotely (applied to the non-exercising limb). Local IPC has been shown to improve VO₂ max and power output by 3% and 4% respectively, during incremental cycling tests, 5 km time trial (TT) treadmill running performance by 2.5%, and exercise capacity in time to exhaustion cycling tasks by 8% to 15.8%. Successful improvements in exercise performance or capacity following RIPC include: handgrip exercise time to exhaustion; rowing 1000 m TT performance and underwater swimming distance. It remains unclear whether applying occlusion directly to the exercising limbs is more beneficial compared to occlusion in the non-exercising limbs.

Timing prior to performance Following completion of IPC, the ‘rest’ duration prior to starting exercise varies across studies ranging from 5 to 90 minutes. Of all practical considerations, rest-to-work duration has arguably been given the least attention as a potential mediator of IPC-induced changes in exercise performance. The influence of rest duration on aerobic exercise performance enhancement is currently unclear, however longer rest time and effect size of anaerobic performance improvement shows a linear relationship.

PRACTICAL ISSUES TO DATE There are some key practical considerations when applying IPC. To date, variation in exercise performance following IPC is likely to be the result of inconsistencies in its use prior to exercise. Further investigation into IPC dose-response, cuff placement, occlusion area and the amount of time needed between exercise and IPC may offer vital insight, allowing athletes to maximise any performance enhancing stimulus that occurs.

IPC dose Doses of 3 x 5 minute or 4 x 5 minute occlusion bouts have been performed. While these doses have resulted in both beneficial and negligible exercise performance findings, a recent systematic review and meta-analysis suggests that use of either 3 or 4 sets of IPC is equally effective with regard to exercise performance outcome. The question still arises as to how to best use this strategy (how to actually perform IPC) in order to achieve optimal results.

Table 1: Practical applications.

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tendency (i.e. the longer the rest, the better the performance)\(^a\). If the mechanisms responsible for improved tissue protection are also responsible for improvements in exercise performance, it would seem the manipulation of rest duration would serve no benefit, as cardio-protection is immediately active following acute IPC exposure and lasts for approximately 2 to 4 hours\(^{20,21}\). No study has previously investigated different rest periods prior to either aerobic or anaerobic exercise bouts, making it difficult to clarify the impact rest duration has on exercise performance. Further studies are required to determine the effect of the length of the rest period between IPC and exercise.

WHICH SPORTS MAY BENEFIT FROM IPC AND WHY?

**Apnoeic sports (breath-hold sports)**

To date, there are three studies investigating the effect of IPC on exercise capable of inducing static or dynamic apnoea. The first study assessing the effects of RIPC on swimming performance found a significant improvement in 100 m swimming time (0.7 seconds), but no change in repeated 200 m efforts\(^{13}\). The improvement in sprint swimming was not matched with alterations in lactate, leading the authors to speculate whether RIPC has the ability to improve mitochondrial metabolism, something which has yet to be confirmed in any human exercise models.

A well-designed study recently found 6 x 50 m maximal swimming sprint performance was significantly improved following IPC (3 x 5 minutes at 220 mmHg), but not following placebo (SHAM) or control trials\(^{22}\). The SHAM condition consisted of 2 x 2 minute cuff inflation periods at 10 mmHg separated by a 1 minute occlusion bout at 220 mmHg. Doing this allowed participants to experience similar perceptual pain without inducing changes in muscle oxygen saturation or stimulating ischaemia-induced tissue protection\(^{22}\). IPC augmented swimming velocity without altering stroke rate, stroke length or number of breaths, implying improved muscular work, which is also reported in cycling exercise\(^{17}\).

The third study concluded muscle ischaemia is an important preparation for physical activity, after finding IPC (performed on one forearm) enhanced static breath-hold by 17% and underwater swimming distance (dynamic apnoea) by 8%. In this study by Jean St Michel et al, underwater swimming distance was improved without an increased time under water, again suggesting an improvement in metabolic efficiency.

**Non-apnoeic sports (Non-breath-hold sports)**

The entrained nature of breathing is often not present in land-based performance tasks. Nevertheless, to date there are 11 studies reporting significantly improved exercise performance in activities such as cycling to exhaustion, repeated Wingate tests, rowing TT performance, 5 km treadmill running TT performance, resistance exercises, isometric leg exercises and handgrip time to exhaustion tasks\(^{23,24,25}\). In contrast, nine studies show negligible changes in exercise performance tasks including repeated sprint ability (running and cycling), 5 km track TT running and incremental cycling to exhaustion\(^{26,27}\). The reason for variation in land-based exercise performance remains unknown. Although, it was reported that there is an overall positive effect on both aerobic and anaerobic (defined by authors as > 30 seconds) exercise, while sprint (defined by authors as < 30 seconds) exercise showed no positive response following IPC exposures\(^{11}\).

It may well be that an optimal exercise intensity exists, independent of modality, to match any physiological/mechanistic changes that potentially prime the body for exercise following IPC exposures. As it stands, non-apnoeic performance results remain relatively unclear after the administration of IPC compared to apnoeic

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**Figure 1:** IPC protocol overview detailing how bilateral IPC takes place. Five minutes of blood flow restriction followed by 5 minutes of cuff deflation take place (usually for 3 or 4 cycles). Once IPC has finished, participants wait for a given time (usually around 30 minutes) before commencing the exercise task. In this case, a 375 kilojoule cycling time trial bout (data taken from our laboratory) was performed and speed, power, heart rate and cadence is displayed. W=watts, BPM=beats per minute, RPM=revolutions per minute.
sport performance, although it should be acknowledged there is an extremely limited number of research publications investigating the effects of IPC on apnoeic sports performance to date.

WHY WOULD IPC HELP AN ATHLETE PERFORM?

Blood flow and vascular responses

Besides the novel suggestion of altered cardiac biomarker response28, there is currently no evidence to suggest IPC can alter cardiac function during exercise, suggesting any changes in blood flow or oxygen delivery during exercise are primarily mediated through changes in vascular function11,12,27,29,30. A remote preconditioning effect reportedly occurs following high-intensity or interval exercise, but not continuous exercise31. Interval exercise prevents endothelial reperfusion injury, preventing a 40% reduction in flow-mediated dilation in healthy individuals following 20-minute upper body prolonged ischaemia. It is proposed that IPC can mimic these results through inducing similar patterns of muscle deoxygenation31, de-saturation15 and a larger shear stress response30; all of which contribute to improved endothelial function.

The extent to which IPC can contribute to blood flow changes during exercise in skeletal muscle is still unclear. RIPC increases skeletal muscle blood flow during reperfusion following prolonged ischaemia, preventing reductions in flow-mediated dilation following high-intensity exercise39. In contrast, when handgrip exercise to failure was improved following RIPC vs placebo (SHAM) (198 ± 70 vs 179 ± 66 seconds, respectively), additional feedback from ultrasound Doppler and near-infrared spectroscopy showed no improvements in blood flow or microvascular balance between oxygen utilisation during the exercise bout39. The maintenance of endothelial function following 5 km TT running, suggests improved exercise performance may be related to improvements in nitric oxide bioavailability34,14. Enhanced nitric oxide levels reduce both local and systemic muscular oxygen cost during exercise34,31 through alterations in skeletal muscle mitochondrial efficiency34. While there was no change in blood flow in a short handgrip time-to-exhaustion protocol39, the mechanistic insight to blood flow response during large muscle-mass exercise remains unknown, especially during high-intensity, strenuous exercise, where performance may become limited by blood flow30.

Skeletal muscle adaptation

Recently, three key studies have reported enhanced skeletal muscle deoxygenation dynamics paired with significantly improved exercise performance (time to exhaustion). It therefore appears that alterations in oxidative mitochondrial metabolism with IPC may be a key mechanism underpinning improved exercise performance. Recently, Cruz et al19 found an 8% improvement in cycling to exhaustion at peak power output that was matched to an IPC-induced improvement in amplitude of the VO2 slow component, rather than accelerated phase II oxygen kinetics, as previously hypothesised. The authors speculated that this may spare a portion of finite anaerobic energy stores during the cycling bout. This hypothesis is partly supported by Kido et al18 who suggested IPC may partially reduce the skeletal muscle oxygen cost following findings of an IPC-induced reduction in the amplitude of deoxyhaemoglobin/deoxymyoglobin during moderate-intensity cycling exercise.

Interestingly, both high-intensity exercise and IPC cause large amounts of shear stress on the endothelial wall, in turn leading to augmented nitric oxide production, derived from endothelial nitric oxide synthase. While supplementation of nitric oxide metabolite compounds and increased nitric oxide bioavailability is beneficial to exercise performance, it also reduces local muscular oxygen cost by improving energy efficiency in the mitochondria34. Therefore, we might speculate that improvement in skeletal muscle energy production is related (at least in part) to local shear-stress-related mechanisms. Similarly, high-intensity exercise prior to competition induces a priming response in the form of accelerated
muscle oxygen response and associated mitochondrial enzymatic activation in skeletal muscle.

Interestingly, excess capacity of mitochondrial respiration, when compared to in-vivo VO2 max only exists during maximal exercise. It would therefore seem that, during maximal aerobic exercise, an improvement in oxygen delivery, not mitochondrial function, may be key in improving performance. Effects of IPC on mitochondrial flux capacity during exercise is currently unclear and warrants further investigation, via both in-vivo and in-vitro muscle biopsy samples.

Nervous system

Enhanced vastus lateralis activation (measured with electromyography) following IPC suggests positive alterations in central nervous system activity. It was hypothesised that inhibition of spontaneous discharges from opioid-mediated muscle afferents could result in an overshoot in central motor drive allowing a higher proportion of skeletal muscle recruitment to take place during intense exercise bouts. Neurally-mediated alterations that occur following IPC have, to date, only been documented in clinical research, with the neural pathway being a proposed route of IPC-induced tissue protection following a prolonged ischaemic stimulus. However, the concept of IPC-induced nociceptive alteration (at either the muscular level or in the nervous system) is certainly intriguing when relating to feedback mechanisms during high-intensity, demanding exercise. While potentially being a damaging adaptation for pacing, it could benefit events which require all out work for extremely short periods (< 4 minutes).

FUTURE IPC DIRECTIONS AND APPLICATIONS

As ischaemic preconditioning continues to show promise in the laboratory environment, organisations may look to employ IPC interventions with development squads, where there may be a greater margin for testing new performance-enhancing strategies prior to competitions. Until data are collected in these more elite populations, it is only possible to speculate on how and when IPC might be used in the elite setting. Current scientific data suggest competitors in apnoic sports may likely benefit from this intervention, with research to date focusing on competition-specific performance tasks.

While observations such as improved cycling time to exhaustion tasks provide promising insight to altered physiological capacity, that in itself may not carry enough specificity to support the use of IPC in land-based athletes (cyclists and runners) prior to important competitions.

References

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