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The effect of intermittent lower limb occlusion on recovery following exercise-induced muscle damage: a randomized controlled trial

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Abstract

Objectives: The purpose of this investigation was to examine the effectiveness of intermittent lower limb occlusion in augmenting recovery from exercise induced muscle damage (EIMD) in physically active males.

Design: Randomized Controlled Trial, double blind

Methods: Sixteen healthy recreationally active male participants were randomly assigned to an intermittent occlusion (OCC; n = 8) or control (SHAM; n = 8) group. The EIMD protocol comprised of 100 drop-jumps, from a 0.6m box. Indices of muscle damage were creatine kinase (CK), thigh-circumference (TC), muscle soreness (DOMS), counter-movement jump (CMJ) and maximal isometric voluntary contraction (MIVC). Measurements were assessed pre, 24h, 48h and 72h following exercise.

Results: There was a significant time effect for all indices of muscle damage suggesting EIMD was present following the exercise protocol. The decrease in MIVC was significantly attenuated in the OCC group compared to the SHAM group at 24 (90.4 ± 10.7 vs 81.5 ± 6.7%), 48 (96.2 ± 6.1 vs. 84.5 ± 7.1%) and 72h (101.1 ± 4.2 vs. 89.7 ± 7.5%). The CK response was reduced in the OCC group at 24 (335 ± 87 vs. 636 ± 300 IU) and 48h (244 ± 70 vs. 393 ± 248 IU), compared to the SHAM group. DOMS was significantly lower in the OCC compared to the SHAM group at 24, 48 and 72h post EIMD. There was no effect of OCC on CMJ or TC.

Conclusions: This investigation shows that intermittent lower limb occlusion administered after a damaging bout of exercise reduces indices of muscle damage and accelerates the recovery in physically active males.

Key Words: muscle function, ischemia, vascular occlusion, delayed onset muscle soreness, eccentric exercise.

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Introduction

Strenuous or unaccustomed exercise involving eccentric muscle contractions leads to exercise induced muscle damage (EIMD) [1]. Typically EIMD manifests as structural damage within the muscle including disruption to sarcomeres and dysfunction of excitation-contraction coupling [2]. EIMD also results in reduced ability for muscle force production, decreased ability to produce explosive muscle contractions, increased muscle swelling, pain and an increase in appearance of muscle proteins in the blood such as creatine kinase (CK) in the days following exercise [1]. Various strategies have been investigated as a methods to attenuate the negative effects of eccentric contractions, including reduced physical function. Therapies attempting to reduce EIMD include antioxidants [3], non-steroidal anti-inflammatory drugs [4], cryotherapy [5] and compression garments [6]. The effectiveness of these therapeutic strategies in reducing signs and symptoms of EIMD is unclear.

Recently, the use of intermittent vascular occlusion (OCC) has come to attention in aiding the recovery process [9]. This involves periods of intermittent vascular occlusion of a limb for short periods of time (2-5 minutes), followed by reperfusion. This process also known as ischemic pre- or post-conditioning has been used to protect cardiac and skeletal tissue against ischemic reperfusion (IR) injury [10]. IR injury is the damage that occurs when blood supply returns to the tissue after a period of prolonged ischemia, causing metabolic and contractile damage [11]. This metabolic and contractile damage observed following IR injury, is similar to that seen in EIMD, namely increased intracellular calcium concentrations [12] and an increase in appearance of muscle proteins in the blood and cytokine markers such as CK, lactate dehydrogenase and IL-6 [11; 13]. OCC can attenuate IR injury and thus may potentially be used to speed up the recovery process following EIMD, via increased blood flow due to its effects on activating ATP-sensitive potassium channels [14], elevating adenosine levels [15] and / or reducing the inflammatory response [16], yet the exact mechanisms are currently unknown.

Whilst OCC may attenuate the functional and metabolic damage associated with EIMD, few studies have studied the efficacy of this intervention on recovery. Unilateral OCC applied following a training session resulted in beneficial effects on functional measures of athletic performance, including repeated

sprint ability and jump height, 24 hs following the intervention [9]. This was the first study to demonstrate a potential use of OCC in the recovery process from athletic efforts. More recently Northey and colleagues [17] applied OCC following a heavy strength training session and found that it did not improve recovery at 1 and 24 h post exercise, when compared to a passive recovery. Therefore evidence for OCC as a recovery tool is conflicting.

To summarize, OCC is recognized as an effective and reliable protective strategy in human cardiac and skeletal muscle, reducing the negative side effects of IR injury. The mechanisms by which damage occurs following ischemia are comparable to those seen following EIMD [1]. Therefore the aim of this investigation was to determine if OCC could enhance the recovery process following EIMD. It was hypothesised that OCC would attenuate the markers of EIMD during recovery in healthy recreational males.

METHODS

Sixteen healthy recreationally active male participants (age, 22.6 ± 2.8 yr; height, 179.6 ± 5.8 cm; mass, 75.5 ± 8.1 kg; mean ± SD) volunteered to take part in the study. The design, implementation and reporting of this study conforms to the Consolidated Standards of Reporting Trials (CONSORT) guidelines for randomized trials. Participants were fully informed of all procedures and associated risks before giving their written informed consent. Participants were randomly assigned to one of two independent groups, OCC or SHAM, in a double blind fashion. Inclusion criteria included an ability and willingness to abstain from strenuous exercise, caffeine, alcohol and anti-inflammatory medication for 72 hours before and for the duration of the study. Exclusion criteria included recent use of other pain management methods, previous history of cardiovascular disease and any lower limb musculoskeletal injuries in the past 6 months. All experimental procedures were approved by the ethics committee of St Mary's University, London, which conformed to the Declaration of Helsinki.

The participants were required to attend the laboratory on five separate occasions based around a 10 day testing period. All trials were performed at the same time of day. In the initial trial, participants were required to attend a familiarization session of all the performance tests. Seven days later,

participants reported to the laboratory for four consecutive days. The first day involved baseline performance tests and completing the EIMD protocol; immediately followed by post exercise tests and the intervention or placebo protocols. The indices of EIMD (muscle soreness [DOMS], maximum voluntary contraction [MIVC], thigh circumference [TC] and vertical jump height [CMJ]) were taken pre and post exercise and at 24 h intervals post exercise up to 72 h. CK was measured at all the same time points except immediately post exercise. The rating of recovery intervention (RORI) was only administered and collected immediately post-intervention.

Muscle damage was induced via repeated drop jumps from a box 0.6m in height and has previously been demonstrated to result in EIMD [18]. Prior to commencing the protocol, participants, had to demonstrate the correct technique; coaching was used to ensure safe practice. Participants conducted five sets of 20 repetitions separated by a two minutes of recovery to ensure maximal intensity was maintained throughout. Participants stepped off the box with their dominant leg, hands on hips and upon landing jumped maximally landing on the same surface.

Upon completion of the EIMD protocol, participants adopted a supine position to allow bilateral arterial occlusion cuffs to be placed on the proximal portion of the thigh (14.5 cm width; Delfi Medical Innovations, Vancouver, Canada). The inflatable cuffs were connected to a pressure gauge and were automatically inflated to either 220mmHg (OCC) or 20mmHg (SHAM) for five minutes followed by five minutes reperfusion. This was repeated three times totalling 30 minutes (15 minutes ischemia and 15 minutes of reperfusion). The pressures chosen have previously been used in similar studies investigating vascular occlusion for recovery [9]. Participants were not informed about the rationale of the study to reduce any placebo effect.

Performance measures for MIVC and CMJ followed a standardised warm-up consisting of five incremental sub-maximal efforts before commencing three maximal efforts separated with 60 seconds recovery. The maximal value was recorded and used for evaluation. This has been quantified to reduce the CV to < 5% [19].

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Knee extension peak torque of the dominant leg was measured via a digital strain gauge (MIE Digital Myometer; MIE Medical Research Ltd. Leeds). Participants were seated in a standardised position with arms folded across their shoulders and both hips and knees flexed at 90º, measured prior to each contraction via a goniometer to minimise error (Bodycare Products, Warwickshire, UK). Participants were required to extend as hard as possible for three seconds [20]. Participants performed a CMJ with hands on hips to assess lower limb muscular power. Participants stood on a portable electronic matt (FLS Electronics Ltd. Jump matt. Ireland) and dropped to a self-selected level (approximately a 90° knee angle) before jumping maximally, jump height, in cm, was used for evaluation. Jump height was calculated from the formula: $h=g \cdot t^2 /8$ (where h is the jump height in metres; g is gravitation acceleration [9.81 $m \cdot s^{-2}$]; t is the flight time in seconds).

Plasma CK was determined from fingertip capillary blood samples. Approximately 300 µl of capillary whole blood was collected ((Microcuvette® CB300, Sarstedt, Numbrecht, Germany) and was immediately placed in a refrigerated centrifuge (Mikro 220R D-78532, Tuttlingen, Germany) and spun at 3,500 rpm for 10 minutes at 4°C. The sample was immediately stored at -80°C for analysis at a later date. All samples were analysed using a semi-automated clinical chemistry analyser (Randox RX Monza Randox, Crumlin, United Kingdom). The normal ranges for plasma CK for this assay are 24-195 IU and the intra sample CV was 2.3%. Muscle swelling was measured on the dominant leg midway between the greater trochanter and the lateral epicondyle of the femur. TC was measured in an anatomical position using an anthropometric tape measure (HaB Direct Southam Warwickshire). To ensure consistent measurements between testing days, TC was marked with a semi-permanent pen [20]. DOMS was assessed via a 200mm visual analogue scale. Participants stood in anatomical position with hands on hips and were asked to hold a half squat (90° knee angle). The far-left of the 200mm line represented ‘no pain’ while the far-right represents ‘extremely painful’. Participants were asked to mark their perceived soreness on the scale [20].

Five minutes post intervention, participants were asked to rate the intervention they received on how they perceived and expected the recovery intervention to encourage the recovery process. This was

measured on a 1–5 Likert scale with one represented 'Like Very Much' and five represented 'Dislike Very Much' [7].

All data are reported as means ± SD. To account for inter individual variation, CMJ and MIVC were expressed as a percentage change relative to baseline. CK, TC, DOMS and RORI data were expressed as absolute values. RORI was analysed using an independent t-test. Differences in the other measured variables were analysed with a mixed factorial two-way repeated measures ANOVA, using treatment as the between subject factor and time as the within subject factor. Where a significant effect was observed, interaction effects were further examined using Fishers least significant difference (LSD) post hoc analysis. All data were analysed using SPSS for Windows (v. 21.0 software package) with the level of significance set at $P < 0.05$.

RESULTS

MIVC was not different between groups at baseline (611 ± 51 vs. 629 ± 136 N, for OCC and SHAM respectively). There was a significant time effect for MIVC, ($P < 0.05$). MIVC showed a significant group ($P < 0.05$) and interaction effect ($P < 0.05$). Post-hoc analysis indicated that the decrease in MIVC was significantly attenuated ($P < 0.05$) in the OCC group compared to the SHAM group at 24 (90.4 ± 10.7 vs 81.5 ± 6.7%), 48 (96.2 ± 6.1 vs. 84.5 ± 7.1%) and 72h (101.1 ± 4.2 vs. 89.7 ± 7.5%) post EIMD (Figure 1).

CMJ was not different between groups at baseline (34.0 ± 4.4 vs. 38.9 ± 8.1 cm, for OCC and SHAM respectively). There was a significant time effect for CMJ ($P < 0.05$) with peak loss in CMJ occurring 24 hours post exercise (84.3 ± 4.3 and 80.0 ± 6.5 % of baseline values for OCC and SHAM respectively). There was no significant interaction ($P = 0.098$) or group effect observed ($P = 0.069$; Table 1).

There was a significant time effect for CK ($P < 0.05$), however there was no significant main effect of group observed ($P = 0.78$). There was a significant interaction between time and treatment for CK ($P <$

0.05), with post hoc analysis revealing CK to be lower in the OCC group at 24 (335 ± 87 vs. 636 ± 300 IU) and 48h (244 ± 70 vs. 393 ± 248 IU) post EIMD when compared to the SHAM group (Table 1).

There was a small but significant time effect for TC ($P < 0.05$), however there was no main group effect observed ($P > 0.05$). TC demonstrated a significant interaction between time and treatment ($P < 0.05$; Table 1), however Post-hoc analysis did not reveal were the differences in TC between OCC and SHAM conditions lay.

There was a significant time effect for DOMS ($P < 0.05$) with peak soreness occurring 24h post EIMD. DOMS demonstrated a significant interaction between time and treatment ($P < 0.05$) and group effect ($P < 0.05$). Post-hoc analysis indicated that the difference in DOMS was significantly lower ($P < 0.05$) in the OCC compared to the SHAM group at 24, 48 and 72h post EIMD (Figure 1).

There was a no difference in the RORI for post-conditioning (mean rank: 2.62 ± 0.92) and control (mean rank: 2.62 ± 0.52) conditions ($P > 0.05$).

DISCUSSION

The primary aim of this study was to examine the effect of OCC on indices of muscle damage following eccentric exercise. The findings confirm our hypothesis that OCC can shorten the recovery process following EIMD, as evidenced by a return to pre strength levels 24 hs earlier than the SHAM condition. This faster recovery of functional outcomes is likely due to a decrease in the inflammatory response observed following strenuous eccentric exercise as observed by reduced creatine kinase and soreness. Thus, OCC promoted a positive environment for reduced muscle soreness and functional recovery in physically active males to a greater extent than a SHAM treatment.

The exercise protocol resulted in EIMD, as evidenced by significant time effects of all dependent variables, supporting the work of others [5, 21]. In the current study we demonstrated MIVC was reduced following EIMD in both conditions, yet the significant group effect indicated the drop in MIVC was attenuated to a greater extent in the OCC group in comparison to the SHAM condition. Post hoc tests

revealed that the loss in muscle strength following EIMD was attenuated across all time points following the application of OCC and returned to pre testing levels within 48 hs. In comparison strength was 90% of pre testing levels in the SHAM condition 72 hs post EIMD. Despite the positive effect on strength recovery, it is not possible to detect whether this was a result of improving the recovery of disrupted sarcomeres in myofibrils and / or damage to the excitation-contraction coupling system.

In addition, the data presented supports previous work that OCC is an effective intervention to enhance the rate of recovery following strenuous exercise [9]. Beaven and colleagues [9] were the first to demonstrate the effectiveness of OCC in the recovery process. It should be noted that whilst improved recovery was observed [9] the exercise protocol and outcome measurements were different from our work. They demonstrated improved recovery 24 hs post-intervention in power production and sprint performance. One more recent study demonstrated that exercise with blood flow restriction may play a role in attenuating EIMD [22] suggesting OCC may be important in preconditioning muscle tissue prior to damage. In contrast we observed OCC was not able to attenuate the decline in lower limb muscular power despite a trend for a group ($p = 0.069$) and interaction ($p = 0.09$) effect. Furthermore Northey and colleagues [17] did not demonstrate any benefit of OCC in the recovery process following strenuous resistance exercise. It is possible that the training status of the individuals may explain the differences between their study and our own. For example, the participants in the current study were recreationally active and therefore MIVC was reduced by 18.5% following EIMD in the SHAM group. In contrast the participants in the Northey and colleagues [17] study had a history of strength training which resulted in a smaller loss of force production (4%), which was likely due to the repeated bout effect [23], suggesting that OCC was less likely to play a role in the trained group.

Our data demonstrates OCC can attenuate the increase in CK as evidenced by reduction at 24 and 48 hs following exercise. CK is an indirect marker of EIMD, which displays a high degree of inter and intra subject variability, mainly due to the training status of the individual [24]. The reduction in CK following the application of OCC suggests cell membrane integrity was maintained to a greater extent than the SHAM group, suggesting a reduction in the inflammatory response to EIMD. A reduction in inflammatory response leads to a reduction in muscle oedema and intramuscular pressure, which

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reduces the stimulation of nociceptors, potentially reducing pain, stiffness and muscle soreness sensations [1].

OCC also had a positive reduction on muscle soreness following EIMD. This is in line with previous research using a similar technique (ischemic preconditioning), which reported reduced postoperative pain following total knee arthroplasty [25]. The mechanism(s) by which OCC might lead to reduced soreness / pain remains elusive. Whilst there was an increased swelling over time, the degree of change was minimal, which is similar to previous studies using this mode of exercise to induce EIMD [8]. Therefore it is likely that the reduced muscle soreness observed following OCC was due to an attenuated inflammatory response to EIMD. Speculatively this may be due to a downregulation of circulating leukocytes [16] and / or increased nitric oxide (NO) which is up-regulated in response to OCC [26], and appears to be an important intracellular and intercellular regulator of muscle inflammation and muscle remodelling [27]. It should be noted however that a reduced inflammatory response may not always be sought. Whilst this may be beneficial for short term recovery, as evidenced in the current study, the inflammatory response is important for adaptations to exercise and thus practitioners should take care as to when they apply different recovery techniques.

A limitation of studies investigating strategies to improve the recovery process is the possible psychological effect of recovery. In both conditions participants were blinded to the rationale of the study. RORI showed no difference between interventions suggesting that the recovery process was due to physiological responses and not psychological mechanisms suggested by others [7, 28]. This suggests that the blinding procedures were successful and their expectations had no effect on other dependant variables. Secondly, participants were recreationally active and therefore the damage they experienced may have been greater than the elite athletic population who would be more accustomed to this type of exercise [23]. Future investigations should aim to further elucidate the mechanisms for improved recovery, including a greater focus on cellular and inflammatory responses. Alongside this research should aim to investigate the dose, frequency and timing of the intervention including the potential impact that OCC has on the adaptation process.

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Conclusion

In conclusion, the data presented in this investigation suggests that the application of 3 x five minutes of arterial occlusion administered following eccentric damaging exercise reduces soreness and enhances post-exercise muscular function. Thus, OCC accelerates the recovery post-exercise in recreational active males, potentially via reduced secondary muscle damage.

Practical Implications

- The current findings contribute to our understanding of recovery from EIMD, which is important for developing appropriate training strategies;
- OCC enhances the recovery process following strenuous eccentric exercise
- OCC may be used by practitioners as a simple and cost effective tool to help athletes recover from exercise.

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REFERENCES

1. Howatson G, van Someren KA. The prevention and treatment of exercise-induced muscle damage. *Sports Med.* 2008;38:483-503. doi:3864 [pii].

2. Byrne C, Twist C, Eston R. Neuromuscular function after exercise-induced muscle damage: Theoretical and applied implications. *Sports Med.* 2004;34:49-69. doi:3415 [pii].

3. Bowtell JL, Sumners DP, Dyer A, et al. Montmorency cherry juice reduces muscle damage caused by intensive strength exercise. *Med Sci Sports Exerc.* 2011;43:1544-1551. doi:10.1249/MSS.0b013e31820e5adc [doi].

4. Tokmakidis SP, Kokkinidis EA, Smilios I, et al. The effects of ibuprofen on delayed muscle soreness and muscular performance after eccentric exercise. *J Strength Cond Res.* 2003;17:53-59.

5. Goodall S, Howatson G. The effects of multiple cold water immersions on indices of muscle damage. *J Sports Sci Med.* 2008;7:235-241.

6. Hill JA, Howatson G, van Someren KA, et al. Influence of compression garments on recovery after marathon running. *J Strength Cond Res.* 2014;28:2228-2235. doi:10.1519/JSC.0000000000000469 [doi].

7. Cook CJ, Beaven CM. Individual perception of recovery is related to subsequent sprint performance. *Br J Sports Med.* 2013;47:705-709. doi:10.1136/bjsports-2012-091647 [doi].

8. Higgins TR, Heazlewood IT, Climstein M. A random control trial of contrast baths and ice baths for recovery during competition in U/20 rugby union. *J Strength Cond Res.* 2011;25:1046-1051. doi:10.1519/JSC.0b013e3181cc269f [doi].

9. Beaven CM, Cook CJ, Kilduff L, et al. Intermittent lower-limb occlusion enhances recovery after strenuous exercise. *Appl Physiol Nutr Metab.* 2012;37:1132-1139. doi:10.1139/h2012-101 [doi].

10. Zhao ZQ, Vinten-Johansen J. Postconditioning: Reduction of reperfusion-induced injury. *Cardiovasc Res.* 2006;70:200-211. doi:S0008-6363(06)00060-5 [pii].

11. Wang WZ, Baynosa RC, Zamboni WA. Therapeutic interventions against reperfusion injury in skeletal muscle. *J Surg Res.* 2011;171:175-182. doi:10.1016/j.jss.2011.07.015 [doi].

12. Warren GL, Lowe DA, Hayes DA, et al. Redistribution of cell membrane probes following contraction-induced injury of mouse soleus muscle. *Cell Tissue Res.* 1995;282:311-320.

13. Chan RK, Austen WG,Jr, Ibrahim S, et al. Reperfusion injury to skeletal muscle affects primarily type II muscle fibers. *J Surg Res.* 2004;122:54-60. doi:S0022-4804(04)00200-8 [pii].

14. de Groot PC, Thijssen DH, Sanchez M, et al. Ischemic preconditioning improves maximal performance in humans. *Eur J Appl Physiol.* 2010;108:141-146. doi:10.1007/s00421-009-1195-2 [doi].

15. Liu GS, Richards SC, Olsson RA, et al. Evidence that the adenosine A3 receptor may mediate the protection afforded by preconditioning in the isolated rabbit heart. *Cardiovasc Res.* 1994;28:1057-1061. doi:0008-6363(94)90275-5 [pii].

16. Konstantinov IE, Arab S, Kharbanda RK, et al. The remote ischemic preconditioning stimulus modifies inflammatory gene expression in humans. *Physiol Genomics.* 2004;19:143-150. doi:10.1152/physiolgenomics.00046.2004 [doi].

17. Northey JM, Rattray B, Argus CK, et al. Vascular occlusion and sequential compression for recovery after resistance exercise. *J Strength Cond Res.* 2016;30:533-539. doi:10.1519/JSC.0000000000001080 [doi].

18. Howatson G, Hoad M, Goodall S, et al. Exercise-induced muscle damage is reduced in resistance-trained males by branched chain amino acids: A randomized, double-blind, placebo controlled study. *J Int Soc Sports Nutr.* 2012;9:20-2783-9-20. eCollection 2012. doi:10.1186/1550-2783-9-20 [doi].

19. Leeder JDC, van Someren KA, Gaze D, et al. Recovery and adaptation from repeated intermittent-sprint exercise. *Int J Sports Physiol Perform.* 2014;9:489-496. doi:10.1123/ijspp.2012-0316 [doi].

20. Howatson G, Goodall S, van Someren KA. The influence of cold water immersions on adaptation following a single bout of damaging exercise. *Eur J Appl Physiol.* 2009;105:615-621. doi:10.1007/s00421-008-0941-1 [doi].

21. Miyama M, Nosaka K. Influence of surface on muscle damage and soreness induced by consecutive drop jumps. *J Strength Cond Res.* 2004;18:206-211. doi:10.1519/R-13353.1 [doi].

22. Sieljacks P, Matzon A, Wernbom M, et al. Muscle damage and repeated bout effect following blood flow restricted exercise. *Eur J Appl Physiol.* 2016;116:513-525. doi:10.1007/s00421-015-3304-8 [doi].

23. Howatson G, Van Someren K, Hortobagyi T. Repeated bout effect after maximal eccentric exercise. *Int J Sports Med.* 2007;28:557-563. doi:10.1055/s-2007-964866 [doi].

24. Clarkson PM, Sayers SP. Etiology of exercise-induced muscle damage. *Can J Appl Physiol.* 1999;24:234-248.

25. Memtsoudis SG, Stundner O, Yoo D, et al. Does limb preconditioning reduce pain after total knee arthroplasty? A randomized, double-blind study. *Clin Orthop Relat Res.* 2014;472:1467-1474. doi:10.1007/s11999-013-3106-4 [doi].

26. Rassaf T, Totzeck M, Hendgen-Cotta UB, et al. Circulating nitrite contributes to cardioprotection by remote ischemic preconditioning. *Circ Res.* 2014;114:1601-1610. doi:10.1161/CIRCRESAHA.114.303822 [doi].

27. Tidball JG. Inflammatory processes in muscle injury and repair. *Am J Physiol Regul Integr Comp Physiol.* 2005;288:R345-53. doi:288/2/R345 [pii].

28. Minett GM, Duffield R. Is recovery driven by central or peripheral factors? A role for the brain in recovery following intermittent-sprint exercise. *Front Physiol.* 2014;5:24. doi:10.3389/fphys.2014.00024 [doi].

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Figure Legends

Figure 1. Consort diagram of enrolled participants

Figure 2. Maximal isometric voluntary contraction (MIVC) before and following EIMD. Values are expressed as mean ± SD. ■OCC, □SHAM. * Indicates significantly different from SHAM, $P < 0.05$.

Table Legends

Table 1. Measures for OCC and SHAM groups; counter movement jump (CMJ), perceived muscle soreness (DOMS), plasma creatine kinase (CK) and thigh circumference (TC) assessed pre, post, 24, 48 and 72h after EIMD. Values are expressed as means ± SD. * Indicates significantly different from SHAM, $P < 0.05$.

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Table 1.

CMJ (% Baseline)	OCC	100 ± 0	85.1 ± 7.3	84.3 ± 4.3	87.0 ± 8.2	87.5 ± 3.1
	SHAM	100 ± 0	84.7 ± 5.2	79.8 ± 6.5	80.5 ± 8.7	82.3 ± 8.1
DOMS (mm)	OCC	8.9 ± 8.0	47.1 ± 25.7	57.0 ± 24.6*	51.4 ± 30.6*	24.5 ± 20.7*
	SHAM	15.6 ±12.5	68.1 ± 31.8	106.1 ± 30.1	99.5 ± 40.4	64.5 ± 37.6
CK (I/UL)	OCC	163.5 ± 30.1		335.8 ± 87.3*	243.8 ± 69.6*	211.8 ± 68.4
	SHAM	178.4 ± 61.4		636.4 ± 300.1	393.2 ± 248.0	335.1 ± 244.1
TC (cm)	OCC	53.9 ± 3.1	54.8 ± 3.0	54.1 ± 3.1	54.0 ± 3.0	53.8 ± 2.8
	SHAM	54.1 ± 4.4	54.9 ± 4.6	54.7 ± 4.3	54.8 ± 4.2	54.6 ± 4.3

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Figure 1

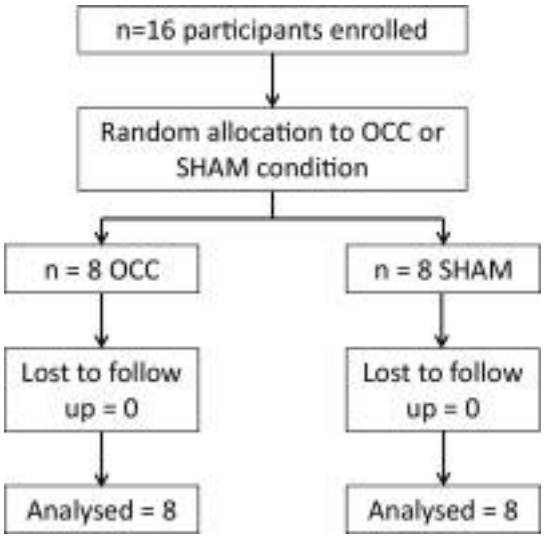

Figure 2