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RITSUMEIKAN UNIVERSITY

A kickoff meeting for the foundation of joint research on sports and health sciences

-Striving for the international science hub-

Faculty of Sport and Health Science, Ritsumeikan University

Ritsumeikan University Global Research Collaboration Support Program 2020

More than just healthy bones: The role of the Vitamin D/Vitamin D receptor (VDR) axis in skeletal muscle

Bollen S, Bass JJ, Smith K, Piasecki M, Brook MS, Phillips BE, Wilkinson DJ, Hewison M, Atherton PJ

Our lab encompasses skill-sets in charting aspects of physical performance, metabolism, and molecular biology in relation to human health. Using state-of-the-art physiological experiments coupled to stable isotope tracers and OMICS, we aim to uncover metabolic and endocrine features of ageing and chronic diseases (particularly those affecting the musculoskeletal system) - and to seek strategies to offset their deleterious consequences. One such area of current focus is that of the Vitamin D axis. While commonly associated with maintaining skeletal health, there is more to vitamin D than just healthy bones[1]. Vitamin D deficiency presents with myopathy, muscle weakness and atrophy, yet the regulatory mechanisms of this hormone in muscle remain poorly defined. The health benefits associated with vitamin D sufficiency are mediated through its receptor (vitamin D receptor (VDR)). Work in cells and rodents under and overexpressing VDR[2,3] suggests that VDR regulates myogenesis, intracellular signalling regulating proteostasis, and also mitochondrial function[4]. Additionally, while it is evident certain genetic variations in the VDR are associated with different skeletal muscle phenotypes, the mechanistic consequences of differences between genotypes are uncertain. This project aims to clarify the mechanistic role of Vitamin D/VDR in muscle by exploring the molecular processes regulated by this axis within myocytes, whilst also exploring the functional consequences of genetic variations within the core vitamin D system.

Keywords: vitamin D, skeletal muscle

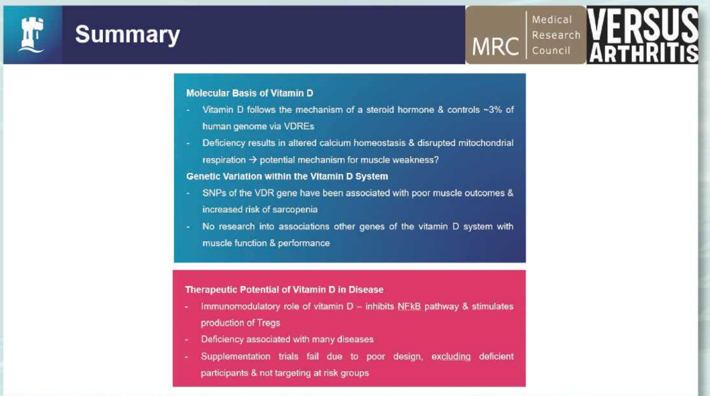
References:

1 Bollen SE, Atherton PJ. Myogenic, genomic and non-genomic influences of the vitamin D axis in skeletal muscle. Cell Biochem Funct. 2021 Jan;39(1):48-59.

2 Bass JJ, Kazi AA, Deane CS, Nakhuda A, Ashcroft SP, Brook MS, Wilkinson DJ, Phillips BE, Philp A, Tarum J, Kadi F, Andersen D, Garcia AM, Smith K, Gallagher IJ, Szewczyk NJ, Cleasby ME, Atherton PJ. The mechanisms of skeletal muscle atrophy in response to transient knockdown of the vitamin D receptor in vivo. J Physiol. 2021 Feb;599(3):963-979.

3 Joseph J Bass, Asif Nakhuda, Colleen S Deane, Matthew S Brook, Daniel J Wilkinson, Bethan E Phillips, Andrew Philp, Janelle Tarum, Fawzi Kadi, Ditte Andersen, Amadeo Muñoz Garcia, Ken Smith, Iain J Gallagher, Nathaniel J Szewczyk, Mark E Cleasby, Philip J Atherton. Over-expression of the vitamin D receptor (VDR) induces skeletal muscle hypertrophy. Mol Metab. 2020 Aug 7;42:101059.

4 Ashcroft SP, Bass JJ, Kazi AA, Atherton PJ, Philp A. The Vitamin D Receptor (VDR) Regulates Mitochondrial Function in C2C12 Myoblasts. Am J Physiol Cell Physiol. 2020 Mar 1;318(3):C536-C541.



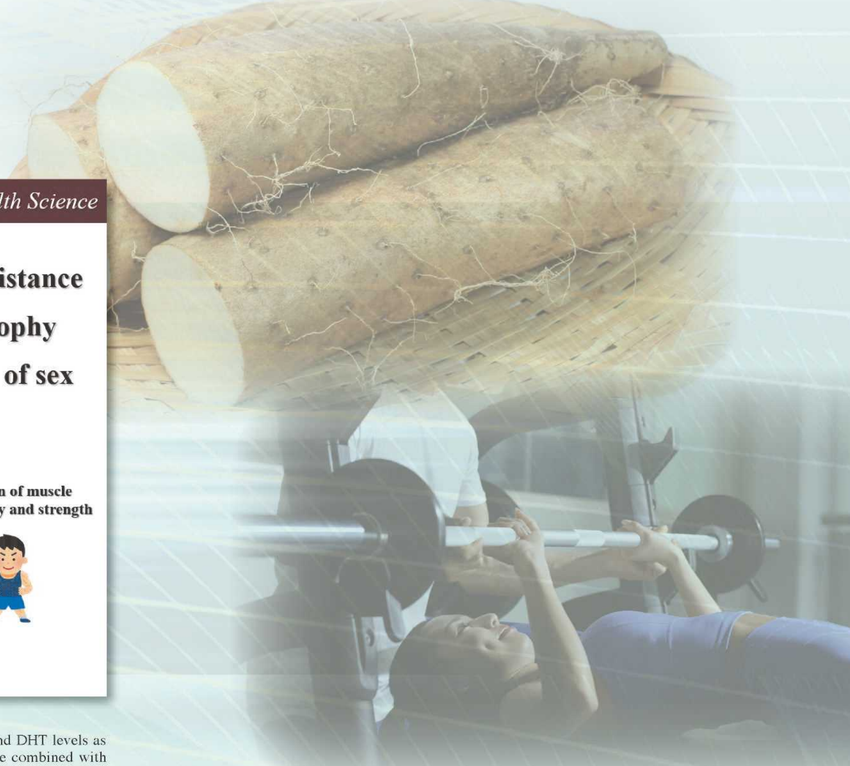
The relationship between the vitamin D system and skeletal muscle remains unclear. Despite evidence suggesting that ~3% of the human genome is under direct control of vitamin D, and certain genetic variations of the vitamin D receptor (VDR) being associated with poor muscle health outcomes, supplementation trials have failed to prove any benefit. This slide summarises the basis for molecular, genetic and disease-associated actions of vitamin D.

Effects of *Dioscorea esculenta* intake with resistance training on muscle hypertrophy and strength in athletes

Horii N, Iemitsu M

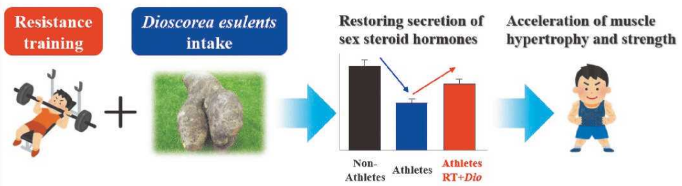
Dr. Iemitsu laboratory investigates that the effects of change in hormones such as myokine and adipokine by exercise training and nutritional intake on improvement of lifestyle-related diseases and acceleration of exercise performance. As one of the hormones, sex steroid hormones such as dehydroepiandrosterone (DHEA), testosterone, and 5α-dihydrotestosterone (DHT) play various important roles in regulation of body composition and acceleration of exercise performance in athletes. The intake of *Dioscorea esculenta*, known as lesser yam, and resistance training have been shown to normalize the secretion of sex steroid hormones in animal studies. This study was to clarify whether *Dioscorea esculenta* intake combined with resistance training would produce effects on muscle hypertrophy and strength in athletes. Male fifteen sprint athletes were randomly divided into 2 groups: 8-week resistance training with placebo or with *Dioscorea esculenta* (2000mg/day) intake. *Dioscorea esculenta* intake combined with resistance training increased the arm lean body mass, the one repetition maximal of snatch and deadlift, and the serum DHEA, free testosterone and DHT levels as compared with resistance training and placebo intake. Thus, *Dioscorea esculenta* intake combined with resistance training has further effects on muscle hypertrophy and strength in athletes by enhancing secretion of sex steroid hormones.

Keywords: Sex steroid hormone, *Dioscorea esculenta*, Resistance training



【Main finding】 *Rits. Univ. Sport and Health Science*

***Dioscorea esculenta* intake combined with resistance training has further effects on muscle hypertrophy and strength in athletes by restoring secretion of sex steroid hormones.**



- Main finding
- Sprint athletes had reduced serum sex steroid hormones such as DHEA, free testosterone and DHT levels as compared with Non-athletes. In the 8-week intervention study, Dioscorea esculenta intake combined with resistance training has further effects on muscle hypertrophy and strength in athletes by restoring secretion of sex steroid hormones.

Atrophy resistant vs. atrophy susceptible skeletal muscles: a new experimental model to study human disuse atrophy

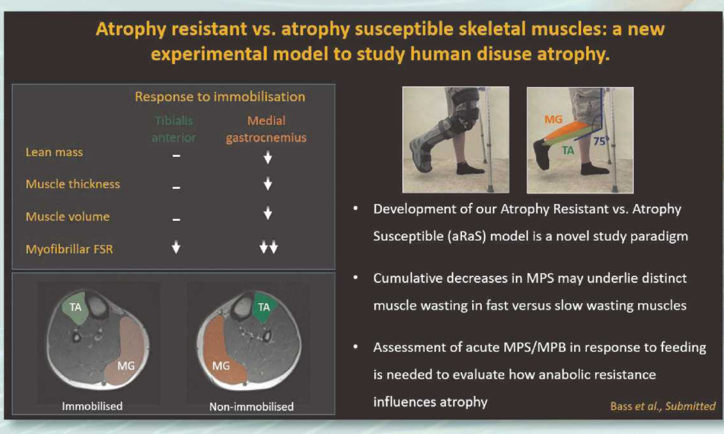
Bass JJ, Hardy EJO, Inns TB, Wilkinson DJ, Piasecki M, Morris R, Sale C, Smith K, Atherton PJ, Phillips BE

Introduction: Muscle wasting through inactivity-induced disuse atrophy (DA) is not fully understood, with not all muscles atrophying to the same degree despite similar roles/locations. Here we used a new approach to investigate the mechanism of DA in humans, developing an experimental model investigating both atrophy resistant and susceptible muscles in the lower leg, i.e. the tibialis anterior (TA) and medial gastrocnemius (MG), respectively.

Methods and results: To investigate this, we recruited seven healthy young men who underwent 15-days single leg immobilisation using a knee and foot brace. Assessment by DXA scans demonstrated after just ~7 days of immobilisation, lower leg muscle mass decreased continuing until day 15. Using MRI and ultrasound scans to study individual muscles, MG size decreased with immobilisation, while TA remained unchanged. D_2O was administered over the immobilisation period, with TA/MG muscle biopsies taken to measure cumulative muscle protein synthesis (MPS). Rates of newly made protein decreased in MG and TA compared to the non-immobilised leg, with MG decreasing at a much greater rate.

Conclusion: The use of this atrophy susceptible vs. atrophy resistant model provides an effective means to study the process of muscle wasting in people, with greater decreases in MPS in atrophy susceptible muscles.

Keywords: Skeletal muscle atrophy, Disuse atrophy



Atrophy resistant vs. atrophy susceptible muscles allows a convenient and effective model to study disuse atrophy, permitting analysis of divergent mechanistic responses of muscle atrophy.

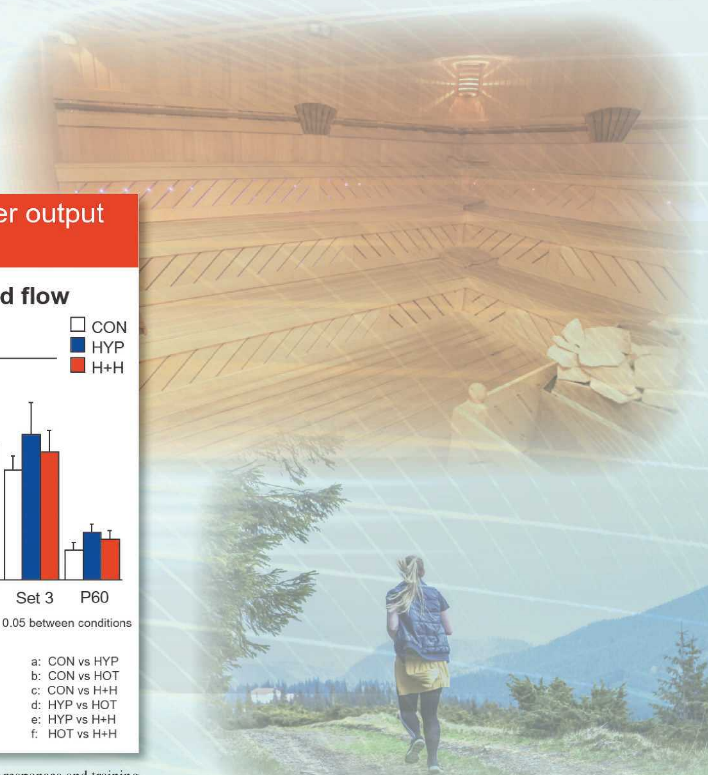
Physiological responses to repeated sprint exercise in a combined hot and hypoxic environment

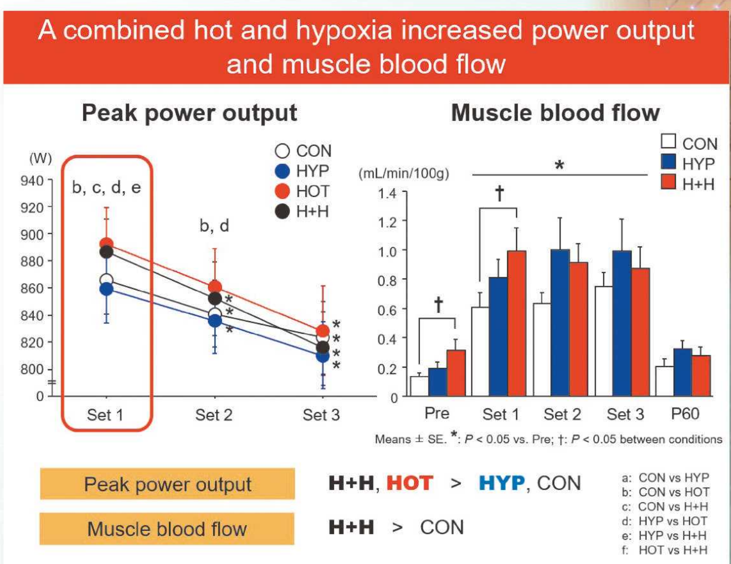
Yamaguchi K, Goto K

In our laboratory (PI: Kazushige Goto, PhD), we have been exploring appropriate exercise training, recovery procedure, and diet for improvement of sport performance as well as health promotion. I have been involved in the research projects to determine the impact of different environmental conditions (e.g., hypoxia, hot, blood flow restriction during exercise).

In the present study, we aimed to determine the effects of a combined hot and hypoxic environment during repeated-sprint training on acute responses and training adaptations. In particular, changes in systemic metabolic variables, muscle oxygenation, muscle blood flow and muscle oxygen consumption in response to a single session of repeated-sprint exercise in combined hot and hypoxic environment were initially evaluated. Consequently, combination of hypoxia and heat stress increased power output and muscle blood flow, but it did not augment muscle desaturation during an acute repeated-sprint exercise session. Furthermore, we compared repeated-sprint performance before and after the 2 weeks of training in hypoxia versus combined hot and hypoxia. However, repeated-sprint training in a combined hot and hypoxic environment did not promote performance improvement compared with the same training in hypoxic environment.

Keywords: normobaric hypoxia, heat stress, repeated-sprint





We examined the effects of a combined hot and hypoxia during repeated-sprint training on acute responses and training adaptations. The combined hot and hypoxia increased power output and muscle blood flow during acute repeated-sprint exercise. However, it did not promote performance improvement compared with the same training in hypoxia.

Neuromuscular adaptations to resistance training: specificity, contributors to strength gain and chronic adaptations

Balshaw TG, Folland JP

Laboratory Overview: Professor Folland directs the Neuromuscular Performance Laboratory at Loughborough University that investigates the integrative determinants of neuromuscular function and the adaptations that occur with exercise, principally resistance training (RT).

Introduction: Dr. Balshaw's presentation will cover three publications that investigated: (1) the extent of training-specific functional and physiological adaptations following short-term explosive- vs sustained-contraction RT; (2) the associations between individual changes in underpinning physiological variables and strength changes after short-term RT; and (3) compared the effect of RT duration (untrained vs. 12-weeks vs. 4-years) on neuromuscular activation (NA).

Methods: Isometric dynamometry, surface electromyography, MRI and ultrasonography were used within these studies to measure strength, NA, muscle volume (MV), and muscle architecture, respectively.

Results and Conclusion: (1) Marked training specificity was observed with early-phase explosive torque (≤100 ms) improvements only occurring after explosive-type RT (+17–34%) due to increased agonist NA. (2) Changes in agonist NA, MV and pre-RT strength combined to explain ~60% of the variance in strength changes after RT, with agonist NA being the greatest single predictor. (3) 12-week and 4-year RT groups had similar maximum agonist NA but antagonist NA was progressively lower with RT exposure and likely continues to adapt with prolonged RT.

Keywords: explosive strength, surface electromyography, quadriceps femoris

CONCLUSION

CENTRE FOR SPORT, EXERCISE & OSTEOARTHRITIS RESEARCH VERSUS ARTHRITIS — Loughborough University

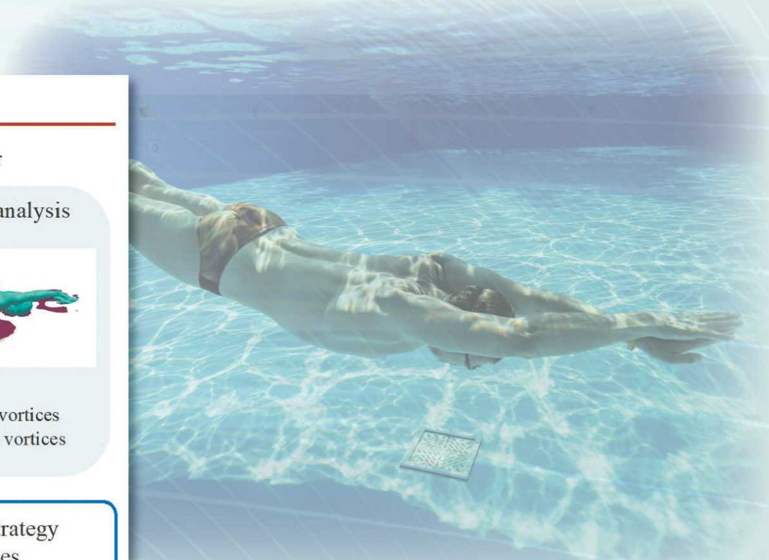
- **(Study 1)** Marked training specific functional, agonist EMG, and hypertrophy were observed between Explosive and Sustained resistance training (RT) **(Balshaw et al., 2016 J Appl Physiol, 120(11), 1364-1373)**
- **(Study 2)** Changes in agonist EMG, muscle volume and pre-RT strength combined to explain ~60% of the variance in strength changes after RT **(Balshaw et al., 2017 Eur J Appl Physiol, 117(4), 631-640)**
- **(Study 3)** 12-week and 4-year RT groups had similar maximum agonist EMG but antagonist EMG was progressively lower with RT exposure **(Balshaw et al., 2019 Scand J Med Sci Sports, 29(3): 348–359.**

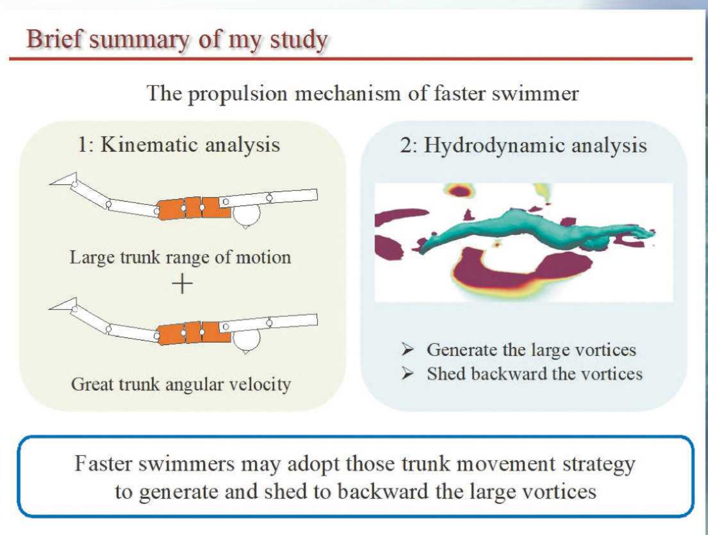
Kinematic and hydrodynamic analyses of underwater dolphin kick

Tanaka T, Isaka T

I belong to the Applied Biomechanics Laboratory of Prof. Isaka, where we focus on the biomechanics for events relating to health promotion, injury prevention, and sports performance. Specifically, I am studying the biomechanics of human swimming for improving swimmers' competitive performance. My research mainly consists of kinematic and hydrodynamic analysis of underwater dolphin kick, which is an underwater propelling maneuver used during the start and turn phases of a swimming race. The underwater dolphin kick has been recently recognized as an important technique for improving race time. In general, swimmers and coaches believe that the trunk angle and angular velocity are the key parameters to generate the greater swimming velocity during the dolphin kick. I investigated whether fast swimmers can utilize specific trunk movement strategies during the underwater dolphin kick, and found that they can generate greater swimming velocity by increasing the trunk angular velocity. In addition, I am analyzing the hydrodynamic mechanics using computational fluid dynamics to investigate the generation and shedding of the vortex abound the trunk. In this meeting, I will present 1) the trunk movement strategy of fast swimmers, and 2) the vortex re-capturing using computational simulation during the underwater dolphin kick.

Keywords: trunk movement strategy, vortex re-capturing, underwater dolphin kick performance





I am studying the kinematic and hydrodynamic mechanics of underwater dolphin kick. I showed the faster swimmers may perform the dolphin kick with greater trunk range of motion and corresponding angular velocity to generate and shed to backward the large vortices.

Program

March 26th, 2021
Location: Online

9:00- 9:05, GMT
18:00-18:05, JST

Greeting

Jin Nagazumi, Dean, Faculty of Sport and Health Science, Ritsumeikan University
Satoshi Fujita, Associate Dean, Faculty of Sport and Health Science, Ritsumeikan University

9:05-11:00, GMT
18:05-20:00, JST

Research Introduction

(2-3 min short introduction by the PI and 10 min research presentation with additional 5 min Q&A for each lab)

①**Philip Atherton,** Professor, Faculty of Medicine & Health Sciences, The University of Nottingham

Shelby Bollen (PhD student)

-More than just healthy bones? The importance of the vitamin D system in skeletal muscle.

②**Motoyuki Iemitsu,** Professor, Faculty of Sport and Health Science, Ritsumeikan University

Naoki Horii (PhD student)

-Effects of Dioscorea esculenta intake with resistance training on muscle hypertrophy and strength in athletes.

③**Bethan Philips,** Associate Professor, Division of Medical Sciences & Graduate Entry Medicine, The University of Nottingham

Joseph Bass (Research Fellow)

-Atrophy resistant vs atrophy susceptible skeletal muscles: a new experimental model to study human disuse atrophy.

④**Kazushige Goto,** Professor, Faculty of Sport and Health Science, Ritsumeikan University

Keiichi Yamaguchi (PhD student)

-Physiological responses to repeated sprint exercise in a combined hot and hypoxic environment.

⑤**Jonathan Folland,** Professor, School of Sport, Exercise, and Health Sciences, Loughborough University

Tom Balshaw (Senior Research Fellow)

-Neuromuscular adaptations to resistance training: specificity, contributors to strength gain and chronic adaptations.

⑥**Tadao Isaka,** Vice Chancellor and Vice President, Professor, Faculty of Sport and Health Science, Ritsumeikan University

Takahiro Tanaka (PhD student)

-Kinematic and hydrodynamic analyses of underwater dolphin kick.