Comparisons of resistance training and 'cardio' exercise modalities as countermeasures to microgravity induced physical deconditioning: New perspectives and lessons learned from terrestrial studies

Authors: James Steele[1,2], Patroklos Androulakis-Korakakis[1], Craig Perrin[1], James Peter Fisher[1], Paulo Gentil[3], Christopher Scott[4], André Rosenberger[5]

[1]School of Sport, Health, and Social Sciences, Solent University, Southampton, UK

[2]ukactive Research Institute, London, UK

[3]Faculty of Physical Education and Dance, Federal University of Goias, Brazil

[4]Department of Exercise, Health, and Sport Sciences, University of Southern Maine, United States of America

[5]Space Medicine Team, ISS Operations & Astronaut Group, Directorate of Human & Robotic Exploration Programmes, European Astronaut Centre, Cologne, Germany

Corresponding author's email: james.steele@solent.ac.uk

Final version published in *Frontiers in Physiology*

Citation for post-print: Steele, J., Androulakis-Korakakis, P., Perrin, C., Fisher, J., Gentil, P., Scott, C., & Rosenberger, A. (2019, September 10). Comparisons of resistance training and 'cardio' exercise modalities as countermeasures to microgravity induced physical deconditioning: New perspectives and lessons learned from terrestrial studies. *Frontiers in Physiology.* 10:1150, doi.org/10.3389/fphys.2019.01150

Abstract

Prolonged periods in microgravity (μG) environments result in deconditioning of numerous physiological systems, particularly muscle at molecular, single fiber, and whole muscle levels. This deconditioning leads to loss of strength and cardiorespiratory fitness. Loading muscle produces mechanical tension with resultant mechanotransduction initiating molecular signaling that stimulates adaptations in muscle. Exercise can reverse deconditioning resultant from phases of de-training, de-loading, or immobilization. On Earth, applications of loading using exercise models are common, as well as in μG settings as countermeasures to deconditioning. The primary modalities include, but are not limited to, aerobic training (or 'cardio') and resistance training, and have historically been dichotomized; the former primarily thought to improve cardiorespiratory fitness, and the latter primarily improving strength and muscle size. However, recent work questions this dichotomy, suggesting adaptations to loading through exercise are affected by intensity of effort independent of modality. Furthermore, similar adaptations may occur where sufficient intensity of effort is used. Traditional countermeasures for μG induced deconditioning have focused upon engineering based solutions to enable application of traditional models of exercise. Yet, contemporary developments in understanding of the applications, and subsequent adaptations, to exercise induced muscular loading in terrestrial settings have advanced such in recent years that it may be appropriate to revisit the evidence to inform how exercise can used in μG. With the planned decommissioning of the International Space Station as early as 2024 and future goals of manned moon and Mars missions, efficiency of resources must be prioritized. Engineering based solutions to apply exercise modalities inevitably present issues relating to devices mass, size, energy use, heat production, and ultimately cost. It is necessary to identify exercise countermeasures to combat deconditioning whilst limiting these issues. As such, this brief narrative review considers recent developments in our understanding of skeletal muscle adaptation to loading through exercise from studies conducted in terrestrial settings, and their applications in μG environments. We consider the role of intensity of effort, comparisons of exercise modalities and the need for concurrent exercise approaches, and other issues often not considered in terrestrial exercise studies but are of concern in μG environments (i.e. O_2 consumption, CO_2 production, and energy costs of exercise).

Post-print article published on 10/09/2019 (doi: 10.3389/fphys.2019.01150) – all authors confirm they are happy to share this work

Introduction

The physiological responses and adaptations to prolonged periods spent in microgravity (μG) environments have been described as a 'classical' topic within the field of environmental and applied exercise physiology (Grassi, 2018). Indeed, the resultant deconditioning of numerous physiological systems and loss of strength, power, and cardiorespiratory fitness is well documented (Bloomberg et al., 2015; Lang et al., 2006; Platts et al., 2014; Tesch et al., 2005; Trappe et al., 2009; Moore et al., 2010). Exercise has long been used as the primary countermeasure for μG induced deconditioning and the history of this has been detailed in an accompanying paper introducing this Research Topic (Scott et al., 2018). Recent reviews (Carpinelli, 2014; Loenneke et al., 2012) have also discussed the considerable attempts to solve the issue of how best to employ this countermeasure in μG environments. Many of these attempts revolve around what could be considered 'engineering based' solutions to employing the traditional exercise modalities often used on Earth as countermeasures for similar deconditioning (e.g. de-training, de-loading, disease, or immobilization). Broadly speaking, exercise is often (though not exclusively) dichotomized into two primary modalities, aerobic training (or 'cardio') and resistance training, with the former primarily thought to stimulate improvements in cardiorespiratory fitness, and the latter thought primarily to stimulate improvements in strength, power, and muscle size. Approaches to solve the issue of performing these typical modalities in μG have included deployment of currently used equipment on the International Space Station (ISS). For example, the Combined Operational Load Bearing External Resistance Treadmill (COLBERT)/Treadmill 2 (T2), Cycle Ergometer with Vibration Isolation and Stabilization System (CEVIS), and Advanced Resistive Exercise Device (ARED) amongst others such as suits for muscle loading (Penguin-3), lower body negative pressure (Chibis), and lower body g-loading (Kentavr), in addition to electrical stimulators (Tonus-3). The different agencies involved have to date employed a range of countermeasure protocols using such devices (Loehr et al., 2015; Yarmanova et al., 2015; Petersen et al., 2016). However, with the planned decommissioning of the ISS in 2024 (the earliest point in time though it may continue past this date), and future goals of manned moon and Mars missions, 'engineering based' solutions to apply both traditional 'cardio' and resistance training exercise modalities inevitably present issues. These primarily relate to the mass, size, energy use, heat production, and ultimately cost of devices. It is therefore necessary to identify exercise countermeasures to combat the losses in strength, power, muscle mass, and cardiorespiratory fitness whilst limiting these issues.

However, this is not a simple task. Research on astronauts actually experiencing μG, particularly over extended periods of time, presents a number of barriers including logistics such as device sizes, costs, and participant sample sizes due to both difficulty in recruiting and the considerable between participant variability in many outcome measures often of interest. As such, 'analogs' for μG environments are often used, with the most common being the bed rest study. A recent issue of *Medicine and Science in Sports and Exercise* detailed the results of NASA's relatively recent 70-day bed rest study. This involved the use of concurrent resistance training and 'cardio' exercise, in addition to testosterone supplementation, as countermeasures to deconditioning in a range of physiological systems (Cromwell et al., 2018; Ploutz-Synder et al., 2018; Dillon et al., 2018; Scott et al., 2018; Murach et al., 2018; Mulvara et al., 2018). The exercise interventions examined in the aforementioned bed rest study have been somewhat influenced by the recent body of literature supporting the use of high effort interval based 'cardio' protocols (i.e. High Intensity Interval Training (HIIT)) as this was implemented as part of the concurrent program. The SPRINT protocol was designed to require less time and be performed at high intensities of effort including: HIIT performed using a custom-built vertical treadmill; resistance training using a custom built horizontal squat device; and both HIIT and resistance training using a flywheel device. Further, work from Russia has historically detailed the countermeasures used with cosmonauts (Kozlovskaya et al., 1995; Kozlovskaya and Grigoriev, 2004; Kozlovskaya et al., 2015) and recently has compared the effects of either treadmill training with alternating sessions of higher and lower effort HIIT (n = 7), or traditional continuous endurance treadmill training (n = 8; Fomina et al., 2016). They examined the cosmonauts over 189±12.4 days aboard the ISS and found the HIIT protocol to result in maintenance of most pre-flight outcomes compared to the losses seen in the traditional endurance training. The Canadian Space Agency (CSA), Japan Aerospace Exploration Agency (JAXA), and European Space Agency (ESA) are currently using similar protocols that have been detailed extensively (Loehr et al., 2015).

It seems that developments within terrestrial studies in exercise physiology have been incorporated into the research programs of those μG analogs. However, other recent work based upon terrestrial studies (Fisher and Steele, 2014) has also begun to question the traditional dichotomy regarding resistance training and 'cardio' exercise, including the need for concurrent training approaches. Furthermore, the same authors suggest that adaptations to loading through exercise may be primarily influenced by the intensity of effort employed independent of modality, and that similar adaptations might be achieved with differing exercise modes assuming sufficient intensity of effort is reached. Indeed, this questioning is of interest to pursue since it could imply that a lower volume of overall exercise might be adequate for astronaut's physical fitness training in μG. Though astronauts value their time for exercise for wider personal wellbeing and many would likely prefer more time for such activity, from an operational perspective any approached that might help reduce time spent exercising could be considered beneficial, particularly if it can also yield similar physiological outcomes compared with greater volumes of exercise.

Contemporary developments in understanding of the applications of, and subsequent adaptations to, exercise induced muscular loading in terrestrial settings have advanced in recent years. It may be appropriate to revisit the evidence to better understand how exercise might be applied in μG for potential investigation in future studies of μG analogs such as bed rest studies. In this brief review we focus on the application of resistance training and 'cardio' training modalities. Topics covered include: the role of intensity of effort, comparisons of exercise modalities (resistance training vs. 'cardio') and whether there is a need for concurrent exercise approaches as currently used as countermeasures, as well as other issues often not considered in terrestrial exercise studies but which are of concern in μG environments such as O_2 consumption and CO_2 production in addition to energy costs of exercise. We note that resistance training and 'cardio' training do not reflect the entirety of possible approaches to exercise countermeasures, nor are cardiorespiratory fitness, strength, power, and muscle size the only outcomes that might be of interest when discussing the deconditioning that occurs in response to μG environments. Scott et al. (2019) list a number of alternative countermeasure approaches in addition to other outcomes of interest in their Introduction to this Research Topic. We encourage the reader to consider the other reviews covered in this Research Topic, which discuss many of these alternative approaches. Further, we add that the recent advances in understanding of exercise response from terrestrial studies presented here should be considered as candidates for further research within μG analogs. Their ability to be effectively implemented into true μG settings not be assumed based upon terrestrial studies.

Intensity of Effort: A Possible Equalizer for Adaptation?

The intensity of effort during exercise can be defined in relation to the current ability to meet the demands of the task being attempted, and for resistance training this is often considered with respect to the proximity to momentary failure (Steele, 2014; Steele et al., 2017). The perception of that effort is thought to arise from the central motor command required to drive the musculature to perform the task being attempted (Marcora, 2009; Pageaux et al., 2016), and of course this drive is influenced by the ability of that musculature to meet those demands, which can be determined by various fatigue processes and afferent feedback from the muscles (Steele and Fisher, 2018). Thus, it is thought that effort, both that required and perceived, is likely intrinsically linked to motor command and motor unit recruitment (de Morree et al., 2012; Guo et al., 2017; Potvin and Fuglevand, 2017).

As noted, it has recently been speculated that, assuming effort is matched, adaptations to exercise are likely to be similar (Fisher and Steele, 2014). Indeed, with respect to resistance training this appears to be the case for muscular adaptations. When performed to momentary failure, recent work suggests there may be little effect of load (Schoenfeld et al., 2017), repetition duration (Schoenfeld et al., 2015; Hackett et al., 2018; Carlson et al., 2018), muscle action (Fisher et al., 2016), or whether 'advanced' techniques are employed such as pre-exhaustion (Fisher et al., 2014), breakdown sets (Fisher et al., 2015), or blood flow restriction (Barcelos et al., 2015; Farup et al., 2015). This is not to say that it is required to train to a maximal intensity of effort (i.e. to momentary failure) to produce adaptation, or that doing so is necessarily optimal; indeed, findings regarding this are conflicting (Davies et al., 2015). Recently, it has also been shown that during high effort but non-momentary failure training there are similar adaptations irrespective of load and that these may even be similar to when training to momentary failure (Nóbrega et al., 2018). It is not clear what the dose-response nature of proximity to failure and thus effort is, or whether a threshold phenomenon might exist to optimize adaptation (Steele

Post-print article published on 10/09/2019 (doi: 10.3389/fphys.2019.01150) – all authors confirm they are happy to share this work

et al., 2017). However, what does seem clear is that when effort is high and appropriately matched, various resistance training manipulations yield very similar adaptations as noted by Phillips and Winett (2010): "…*effort is internal to the person, can be created with a variety of protocols, and is not dependent upon a specific amount of external force*.". As such, effort could be considered in both resistance training and 'cardio' training as being determined primarily with respect to proximity to momentary failure.

The importance of high or maximal intensity of effort has become apparent and studies of concurrent exercise in μG simulations have begun to use these approaches for both 'cardio' and resistance training (Cotter et al., 2015). However, it is not known whether similar effects are seen across modalities when either modality alone is performed. As an example, resistance training has been evidenced to result in improvements in cardiorespiratory fitness (Steele et al., 2012; Ozaki et al., 2013; Ashton et al., 2018), and 'cardio' training to improve strength and muscle size (Konopka and Harber, 2014; Ozaki et al., 2015) though their comparative effects are less clear. Studies have attempted to compare 'cardio' and resistance training modalities, some of which have appropriately controlled for effort, and duration. Others have examined what could be considered more traditional representations of the two approaches. In the following section we will review these studies and consider whether the stimulus and adaptation resulting from exercise induced loading is influenced by the modality used.

Comparisons of Traditional 'Cardio' and Resistance Training Approaches

Traditional approaches to 'cardio' are often performed using locomotive or ergometer tasks (e.g. walking, jogging, running, cycling, rowing, etc.) in a continuous fashion with respect to duration at submaximal intensities of effort commonly determined relative to either maximal heart rate, heart rate reserve, VO_2max, or sometimes using ratings of perceived effort scales. Sometimes they are performed using 'high intensity interval approaches' though many studies that compare modalities still use submaximal intensities of effort and are unmatched compared to the resistance training approaches examined. Contrastingly, resistance training is often performed with external resistance of varying degrees relative to maximal strength provided by either free weights, machines, bodyweight, or some other implements (e.g. resistance bands), either with single or multiple sets of repetitions which may or may not be performed to momentary failure (but are often performed to a relatively high effort). Most people would recognize these approaches as being 'ecologically valid' implementations of either 'cardio' or resistance training (i.e. reflective or their implementation in 'real-life' settings) and numerous studies have compared these forms.

When comparing resistance training and 'cardio' approaches, though some studies suggest no significant differences for changes in cardiorespiratory fitness (Messier and Dill, 1985; Hepple et al., 1997; Sawczyn et al., 2015), the majority suggest that 'cardio' type approaches favor cardiorespiratory fitness increases (Goldberg et al., 1994; Poelhman et al., 2000; Ferrara et al., 2006; Wilkinson et al., 2008; Silanpaa et al., 2008; Athianen et al., 2009). Similarly, for strength changes, though there are exceptions (Messier and Dill, 1985), the majority of research suggests that resistance training produces greater increases in strength than 'cardio' type training (Goldberg et al., 1994; Poelhman et al., 2000; Ferrara et al., 2006; Wilkinson et al., 2008; Silanpaa et al., 2008; Athianen et al., 2009). Furthermore, a recent meta-analysis has also shown that resistance training produces more favorable changes in muscle hypertrophy compared to 'cardio' type approaches (Grgic et al., 2018).

This body of research suggests a specificity of training response with respect to 'cardio' and resistance training, with the former favoring cardiorespiratory fitness and the latter favoring strength and hypertrophy. However, these results apply to broad comparisons of these two ecologically valid approaches to training. Yet the results of the aforementioned comparative studies do not necessarily imply that the modality, and thus mechanical resistance (e.g. the load on a resistance exercise, or the power output on a cycle ergometer) itself independent of the manner in which exercise is performed with it, is influential with respect to adaptations. Many of the studies cited have often tested their outcomes in manners that might favor particular interventions. For example, cardiorespiratory fitness being tested on the modality for which the 'cardio' intervention was trained, and conversely strength being tested as a one repetition maximum in the exercise for which the resistance training intervention was specifically trained. Further, as noted, in none of the aforementioned comparative studies were attempts made to control for the effort and duration of the two interventions. However, there has in recent years been attempts to conduct research comparing across exercise modalities whilst controlling for effort and duration examining both the acute physiological responses in addition to the chronic physiological adaptations.

Effort and Duration Matched Modality Comparisons

A number of studies have examined the influence of modality upon acute responses, typically focusing upon measures which may be speculated to have a potential role in mediating chronic adaptations. Vilaça-Alves et al. (2016) compared both upper and lower body 'cardio' (upper- and lower-body cycle ergometry) and resistance exercise (smith machine bench press and smith machine half squat) modalities during low intensity of effort with physiologically matched tasks (demands eliciting 4mmol$\cdot$L^{-1} of blood lactate). They examined the oxygen uptake responses between the two modalities finding no differences and concluded that the manner of exercise performance, and not the modality, was likely the primary determinant of this physiological response. More recently, Steele et al. (2018) compared the acute response of lower body 'cardio' (recumbent cycle ergometry) to resistance exercise (leg press) during high intensity of effort tasks, matched for effort and duration (4 x 60s sprints for 'cardio' and 4 x 12 repetition maximum for resistance exercise with time matched using a 2s concentric and 3s eccentric repetition duration). They considered a range of physiological responses including oxygen consumption, respiratory exchange ratio, blood lactate, estimated energy expenditure, muscle swelling, and electromyography finding no differences between the modalities for any outcome. Steele et al. (2018) examined only amplitude based electromyographical variables but Noble et al. (2017) have also examined normalized (to % max) electromyographic amplitudes which appear to be greater during typical resistance training (single leg knee extension) compared with `cardio' mode (single leg cycle ergometry) exercise performed to volitional failure. Unlike Steele et al. (2018), time to task failure in Noble et al. (2017) was unclear and thus, it is unknown if it was similar between conditions. Amplitude based analyses may not reflect the entirety of motor units recruited where task durations differ, particularly if differing recruitment patterns are occurring (i.e., sequential recruitment of low to high threshold during low force tasks, and simultaneous recruitment of both low and high threshold motor units during high force tasks; Fisher, Steele & Smith, 2017; Vigotsky et al., 2017; Potvin & Fuglevand, 2017; Enoka & Duchateau, 2015). However, Kuznetsov et al. (2011) examined resistance training (knee extension) and `cardio' exercise (cycling) modalities performed to momentary failure (thus controlling for effort) using frequency based electromyographic analyses and reported that similar recruitment of motor units may occur during both modalities. These findings might be expected considering the possible link between effort and central motor drive as noted above. For example, motor unit recruitment for active muscles might be relative to task demands independent of the exercise modality, which might also be true for other physiological responses such as oxygen consumption, blood lactate production, muscle oedema, etc.

Similarity in acute responses between modalities when effort and duration are matched has led to the hypothesis that the accompanying chronic physiological adaptations may therefore be similar as well (Fisher and Steele, 2014). However, to date, research examining this is limited. Only two studies have been published to our knowledge (Androulakis-Korakakis et al., 2017; Álvarez et al., 2017); though, our lab and others have been conducting research in this area, the initial findings of three further studies are also presented below.

Androulakis-Korakakis et al. (2017) examined an 8 week's intervention of additional (i.e. alongside their normal training) 'high intensity interval training' performed using either a 'cardio' exercise modality (cycle ergometry) or a resistance training modality (squats and deadlifts) in powerlifting and strongman athletes. Both were performed 2x/week for 7 sets of either 30 seconds on the cycle ergometer or sets of ~16-30 seconds alternating with squats and deadlifts at a rating of perceived effort of 8-9 (on a 0-10 scale) and with 90 seconds rest between sets. Predicted VO_2max using the step test and predicted 1 repetition maximum on the knee extension were selected as outcomes to avoid issues of specificity (as discussed above) of training modality affecting test outcomes. Both outcomes improved, yet there were no statistically significant differences between groups[1] for change in predicted VO_2max (Δ = 4.6 ml.kg.min^{-1} [3.0 to 6.3] vs. Δ = 3.4 ml.kg.min^{-1} [1.7 to 5.1] for 'cardio' and resistance training, respectively; $p = 0.259$) or for change in predicted knee extension 1 repetition maximum (Δ = 7.1 kg [4.4 to 9.7] vs. Δ = 6.9 kg [4.2 to 9.5] for 'cardio' and resistance training, respectively; $p = 0.895$). It is

[1] Note, data has been reanalysed using JASP (version 0.9.1, University of Amsterdam, Netherlands) for this study with ANCOVA for the change in outcome (post- minus pre-scores) using pre-scores as covariates.

Post-print article published on 10/09/2019 (doi: 10.3389/fphys.2019.01150) – all authors confirm they are happy to share this work

surprising to see improvements in an already well trained population such as this, and thus, it might be expected that results may translate to untrained populations as well.

Álvarez et al. (2017) recently compared 12 weeks of effort and duration matched `cardio' (cycle ergometer `high intensity interval training') and resistance training (full body resistance training including biceps curls, knee extension, shoulder press, and upright rows) 3x/week in insulin resistant women. Each was performed with the same work:rest intervals (60 s:120 s) for 12 sets at a rating of perceived effort of 8-10 (on a 0-10 scale). Their outcomes included body composition/anthropometry, cardiovascular outcomes, plasmatic concentrations, strength, and endurance. For most of these they found improvements but no statistically significant differences between groups. However, for strength there were greater changes in the resistance training group (see figure 2 below), though strength was tested using 1RM on the same exercises used in training (measured as 1RM in biceps curl, knee extension, shoulder press, and upright row). To the contrary, endurance performance was tested as 2 km walking test which improved in both groups with no statistically significant differences between them (both improving by ~2 minutes; $p = 0.284$).

More recently, Gil-Sotomayor et al. (2018) presented results from a study comparing 12 weeks of 'high intensity interval training' combined with a low carbohydrate high fat diet using either 'cardio' (cycle and/or treadmill ergometer) or resistance training (pull-down, leg press, bench press, dumbbell row, sumo squat, and push-ups) 3x/week. Both were effort and duration matched and performed with the same work:rest ratio (60 s:60 s) for 10 sets each with a target rating of perceived effort of 16-18 (on a 6-20 scale). They reported that VO_2 peak, body mass, fat mass, and visceral fat were all significantly improved in both groups. For VO_2 peak, Hedge's g for changes were 0.57 and 0.53 for 'cardio' and resistance training, respectively. Of note, lean body mass did decrease slightly for the 'cardio' modality (g = -0.07) and did not change for resistance training (g = 0.00).

Finally, our labs are currently completing a training intervention study using a similar approach to the aforementioned acute responses study by Steele et al. (2018) using a within-participant design, in addition to having recently completed a further between-group training intervention study. In this within-participant study, Armes et al. (unpublished) have begun examining lower body 'cardio' (unilateral recumbent cycle ergometry) with lower body resistance exercise (unilateral leg press) matched for effort and duration (4 x 30 s sprints and 4 x ~5-7 repetitions to momentary failure at 2 s:3 s repetition duration for 'cardio' and resistance exercise, respectively). A within-participant design, whereby participants limbs were randomized to conditions in a counterbalanced fashion based upon dominant limb, has been used to increase power and precision for estimates by reducing between-condition variation from independent samples (MacInnis et al., 2017). The training consists of 2 sessions per week for 8 weeks with both conditions performed in each session with the order alternated in order to avoid any specific order effects of performing one condition prior to the other. Outcomes being examined included unilateral VO_2 peak and time to exhaustion during an incremental exercise test on an upright cycle ergometer, unilateral isometric knee extension strength, and ultrasound measured quadriceps muscle thickness. Based on precision (i.e. desired width of confidence intervals set at 0.5 population standard deviation), target N was calculated at 21, though here we present preliminary data for $N = 8$ participants[2] (figure 1). Despite the within-participant design, there is evidently considerable variation or noise in the data. However, at this stage, descriptively it seems that VO_2 peak improves slightly on average with only a small difference between conditions for this change and the same seems to be the case for strength. Time to exhaustion, however, though improving for both conditions has clearly increased to a greater degree in the 'cardio' condition. Although training was performed with a recumbent cycle ergometer and testing was on an upright cycle ergometer, there was sufficient transfer with respect to the specificity of motor tasks that improved time to exhaustion independently of VO_2 peak. Lastly, and likely reflective of the inherent noise in the measures, or individual variation in response, quadriceps muscle thickness did not clearly change for either condition and the average changes seen so far fall within the technical error of measurement for our lab.

[2] Note, one participant did not complete post testing for VO_2 peak and time to exhaustion due to illness and so $N = 7$ for these outcomes.

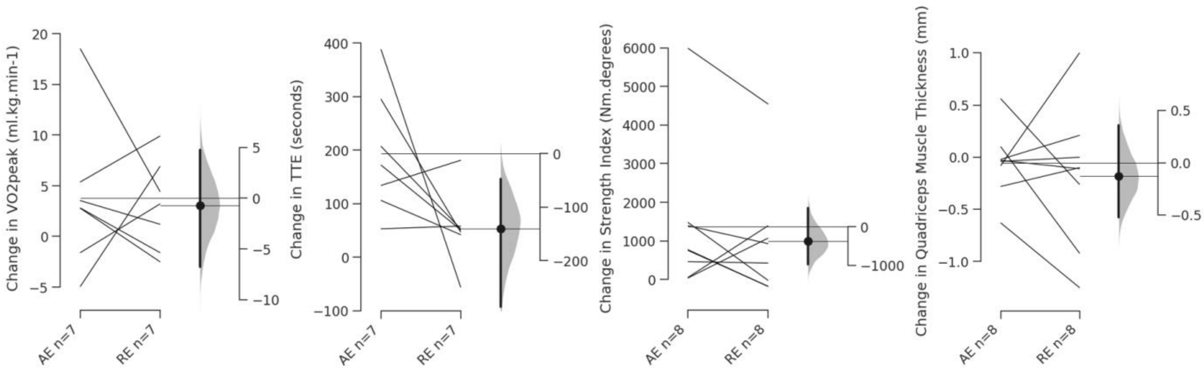

Figure 1. From left to right, individual responses and paired comparisons (floating axis showing mean difference with 95% confidence intervals) for change in VO_2 peak, time to exhaustion during progressive ramp unilateral cycle test, isometric knee extension strength index (area under torque curve), and quadriceps muscle thickness; AE = Aerobic Exercise/'Cardio' Group; RE = Resistance Training Group

The between-group training intervention study completed by Silva et al. (2019) was conducted in trained males (with a minimum of 6 months prior resistance training experience) and using either resistance training on a leg press (4 x ~10-12 repetitions to momentary failure at concentric to eccentric 1 s:2 s repetition duration ratio) or 'cardio' training on an upright cycle ergometer (4 x 30s sprints). Outcomes included strength measured using knee extension 10RM, VO_2peak measured using a maximal incremental treadmill protocol, and body composition measures of the legs using dual X-ray densitometry (DXA). Analysis using ANCOVA with baselines values as covariates revealed no statistically significant between group differences ($F_{(1,22)} = 0.261$, $p = 0.614$) for change in strength with improvements in both the leg press (estimated marginal mean [95%CIs] $\Delta = 10.1$ kg [6.9 to 13.3]) and cycle ergometer (estimated marginal mean [95%CIs] $\Delta = 9.1$ kg [6.1 to 12.2]). There were also no statistically significant between-group differences for changes in total leg mass ($F_{(1,22)} = 1.589$, $p = 0.221$), leg lean mass ($F_{(1,22)} = 0.491$, $p = 0.491$), or leg fat mass ($F_{(1,22)} = 1.238$, $p = 0.278$) and changes within-groups were negligible. For changes in VO_2peak, however, there was a statistically significant between-group difference ($F_{(1,22)} = 5.926$, $p = 0.023$) revealing greater increase for the cycle ergometer group (estimated marginal mean [95%CIs] $\Delta = 5.66$ ml.kg.min^{-1} [2.63 to 8.68]) compared with the leg press group (estimated marginal mean [95%CIs] $\Delta = 1.23$ ml.kg.min^{-1} [-1.92 to 4.38]). Considering the different training and testing modality, this change is interesting and contradicts results reported by others regarding changes in cardiorespiratory fitness measured with a range of tests and using effort matched protocols (Álvarez et al., 2017; Gil-Sotomayor et al., 2018), including those in trained populations (Androulakis-Korakakis et al., 2017). However, the study by Silva et al. (2019) there was considerable variation in maximal criteria from the incremental treadmill protocol with none of the participants reaching a respiratory exchange ratio >1.15 and also a number of participants showing differences in end of test max heart rate (>10 beats.min^{-1}) between pre- and post-tests suggesting that truly maximal efforts may not have occurred. In contrast, all participants that have been tested so far by Armes et al. (unpublished) have met maximal criteria for the incremental exercise test (RER >1.15, hear rate ±10 beats.min^{-1} of age predicted max, Borg scale rating of 20, and blood lactate >8 mmol.L^{-1}).

Considering the pattern of findings from this emerging body of research, there does seem to be evidence supporting the hypothesis of physiological adaptations and responses being primarily determined by effort, and less influenced by modality. In fact, random effects meta-analysis[3] comparing effect sizes between 'cardio' and resistance training modalities for 4 of the studies discussed above (Álvarez et al., 2017; Androulakis-Korakakis et al., 2017; Armes et al., unpublished; Silva et al., 2019) seem to support that presently there is little evidence suggesting a difference between modalities when effort is controlled for. For strength, the effect size favored resistance training only trivially though with moderate precision for the estimate (figure 2) and similarly so for changes in cardiorespiratory fitness measures in 'cardio' training (figure 3). This is an emerging area and despite the similarity of findings across studies there is clearly further work required to approach a more precise understanding of the differences, or lack thereof, in adaptations produced by different yet effort matched modalities. However, the potential implications of what we understand so far are discussed below. For now, we

[3] Performed using the 'metafor' package in R (version 3.5.1; R Core Development Team, https://www.r-project.org/) and an alpha of 0.05 considered in all tests. Between group effect sizes using Cohen's *d* were calculated for differences between groups in change scores, and pooled change score standard deviations used as the denominator (Morris, 2007; Borenstein et al., 2009; Dankel et al., 2018). The study of Gil-Sotomayor et al. (2018) was not included due to data on variance being unavailable. For Álvarez et al. (2017) a single effect size was calculated from the pooled composite of the 4 strength outcomes included. ES for *d* were interpreted with reference to Cohen's (1988) thresholds; trivial (<0.2) small (0.2 to <0.5), moderate (0.5 to < 0.8), and large (>0.8) and positive ES values indicated higher scores of the outcome in favor of the resistance training group.

Post-print article published on 10/09/2019 (doi: 10.3389/fphys.2019.01150) – all authors confirm they are happy to share this work

briefly look to other considerations often overlooked in research considering exercise countermeasures to μG-induced deconditioning.

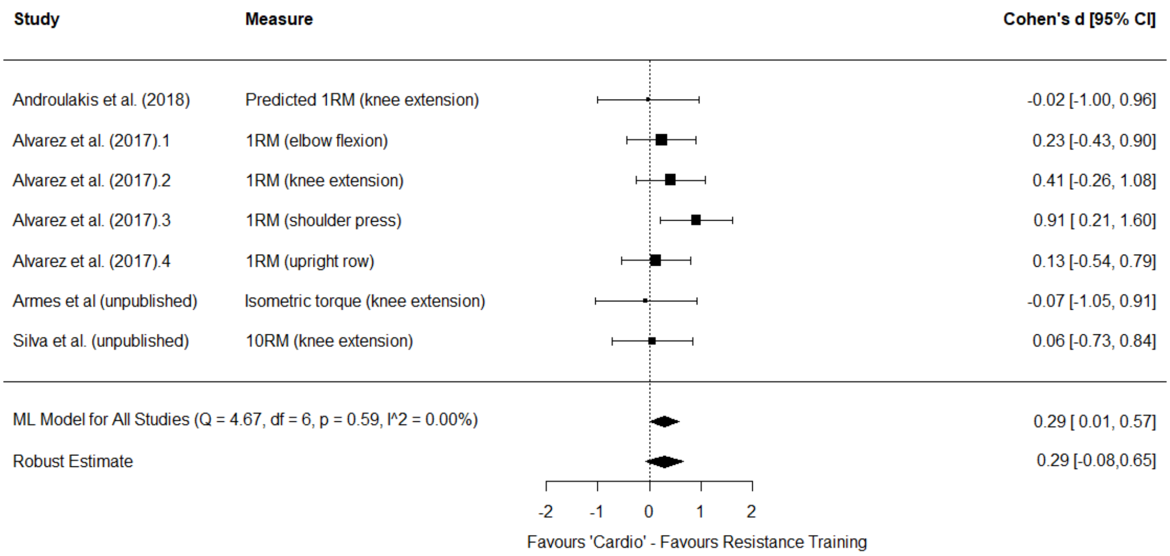

Figure 2. Forest plot for random effects (RE) meta-analysis of strength outcomes from studies using effort matched designs to compare ‘cardio’ and resistance training modalities.

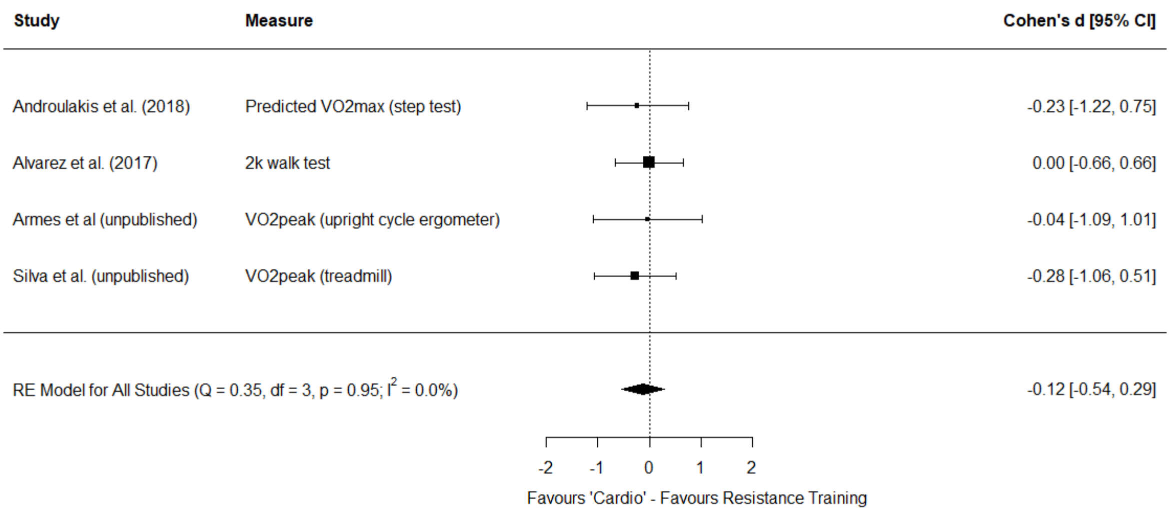

Figure 3. Forest plot for random effects (RE) meta-analysis of cardiorespiratory fitness outcomes from studies using effort matched designs to compare ‘cardio’ and resistance training modalities.

Other Considerations: O_2 Consumption, CO_2 Production, and Energy Costs

Factors which are often underappreciated when considering exercise countermeasures for μG-induced deconditioning are that, compared to rest, exercise increases O_2 consumption, CO_2 production, and energy costs. Combined, the former two mean that more O_2 needs to be produced via electrolysis and additional CO_2 need to be removed. Furthermore, the additional energy expenditure from exercise requires that additional resources are necessary to replenish that energy used by the astronauts (i.e. food rations). This is particularly noteworthy since data shows an increased energy requirement (1.4 x resting metabolic rate) through elevations in basal metabolic rate in both simulated (Acheson, et al. 1995), and μG environments (Stein, et al. 1999). As such, it is of interest to consider the effects of 'cardio' and resistance training upon O_2 consumption, CO_2 production, and energy costs. However, there is little research specifically examining this area, especially that which has controlled for effort and duration of exercise to examine the effects of modality. Work matched comparisons of different resistance training approaches (circuit style or traditional consecutive sets) show that O_2 consumption (aerobic energy expenditure during exercise and rest interval) and total energy expenditure is similar (Aniceto et al., 2013). Although, it is noteworthy that anaerobic energy expenditure estimated from production of blood lactate was higher in consecutive sets compared with circuit style of resistance training suggesting CO_2 production may be higher (Aniceto et al., 2013). Thus, other technical elements of how resistance training protocols are manipulated may be important to consider. For example, consecutive sets of resistance training when performed not to momentary failure likely results in increasing effort with each set due to residual fatigue. Though it would seem that effort may be an important factor impacting the similarity of responses and adaptations to different exercise modalities, Scott and Earnest (2011) have shown that aerobic, anaerobic, and recovery energy expenditures are all higher with resistance training performed to momentary failure even when work is matched. As noted earlier, it appears that O_2 consumption, CO_2 production, and energy costs are more a function of the intensity of effort of exercise as opposed to the modality.

Discussion and Suggestions for Potential Research and Solutions

Though currently there is limited research examining the role of modality of exercise, what has been conducted is suggestive of greater similarity in the physiological responses and adaptations between 'cardio' and resistance training than historical dichotomies would predict, assuming effort and duration are matched. Considering this, the prevailing use of concurrent training modalities on the ISS to counter μG induced deconditioning of physiological systems may be unnecessary. Indeed, of interest is that similar changes can occur even in well-trained participants as reported by Androulakis-Korakakis et al. (2017) and found by Silva et al. (2019) despite the fact that the adaptive response to exercise is attenuated in trained persons. Astronauts undergo considerable physical preparation prior to entering μG environments and then subsequently experience deconditioning akin to that which might occur from a period of detraining. Periods of detraining have been shown to restore sensitivity of anabolic signaling pathways in skeletal muscle (Ogasawara et al., 2013). Thus, considering the similar responses reported in both trained (Androulakis-Korakakis et al., 2017; Silva et al., 2019) and also untrained populations (Álvarez et al., 2017; Gil-Sotomayor et al., 2018) it seems reasonable to speculate that single modality approaches to counter μG induced deconditioning might be appropriate. This could potentially halve the time required by astronauts for engagement in training as a countermeasure and potentially have concurrent impact on reducing volume of space taken up by equipment, as well as reducing O_2 consumption, CO_2 production and energy use by the astronauts in addition to heat production and energy use from exercise devices themselves.

In this sense, it could also be argued that either 'cardio' or resistance training approaches might therefore be chosen as the preferred modality, though we would argue that resistance training approaches in general include further benefits over and above 'cardio' based approaches which we discuss below. As noted, the choice of a single modality may solve issues of time, volume of space, and energy use/heat production. Moreover, resistance training in contrast to 'cardio' approaches can be performed in a manner that better addresses these issues. For example, isometric resistance training has been shown to require lower VO_2 consumption and energy cost compared with dynamic forms (Scott et al., 2015). It can also be performed without the need for external devices ('just' proper fixation in the spacecraft is needed in most exercises). Isometric resistance training can also be performed using contralateral limb provided resistance (i.e. using one limb to resist the movement of the other) which can elicit similar electromyographical activity as traditional free weight training (Fisher et al, 2016). Maximal isometric co-contraction approaches have also been examined and found to be effective for upper limb (Maeo et al., 2014; Maeo et al., 2014) and trunk and hip musculature (Tayashiki et al., 2016), though may be potentially less effective for the lower limbs (Maeo and Kanehisa, 2014). There may be some concerns with the use of isometrics for countering μG deconditioning. Haddad et al. (2006) suggested that their use did not counteract the downregulation of anabolic signaling that occurred from short term unloading, though follow up research from their lab found that, assuming sufficient volume of exercise is performed, signaling is similar independent of muscle action (Garma et al., 2007). This being said, early work has suggested that adaptations to contractile kinetics may differ between isometric and concentric resistance training (Duchateau and Hainaut, 1984) and so perhaps a combination of the two may be best. Other examinations of 'no load' resistance training have been reported showing that dynamic movement coupled with maximal voluntary effort to activate the muscle involved produces high electromyographical activity independent of training status, limb dominance, movement velocity, or the use of visual feedback (Gentil et al., 2017), and such training has been shown to produce similar increases in muscle size and strength compared to traditional dynamic free weight training (Counts et al., 2016). In addition, there are more simple approaches to providing external resistance for dynamic resistance training compared to those primarily used in current μG environments. For example, partner assisted manual resistance training has been shown to be similarly effective to more traditional approaches (Dorgo et al., 2009), however, at least for missions to the ISS where crew time is critical and their schedule is often constrained, this training regimen may be less favorable. Also, a simple self-powered rope trainer has been examined for possible use in μG environments and shown to be equally effective in increasing strength as traditional free weight resistance training (Behringer et al., 2016). Further, even when performed using minimal doses (twice a week using 3 multi-joint exercises performed for two sets to a rating of perceived effort of 8 out of 10 where 10 would be the point of momentary failure), elastic resistance bands have been shown to produce similar strength changes to traditional free weight or machine-based resistance training (Souza et al., 2018).

Thus, there may be the potential to employ resistance training based approaches alone and in such a way where the equipment requirements are further reduced. However, were future research to examine and validate resistance training as an effective single modality in μG analog studies, for it to be considered appropriate as the single modality approach for space missions, other aspects need also to be taken into consideration. We have focused here upon cardiorespiratory fitness, strength, and muscle size as they have been the primary outcomes for terrestrial comparative studies. However, specific performance levels for certain tasks would likely be needed to maintain the ability to perform these specific motor patterns. Without inclusion of at least some walking/running there may be a potential injury risk due to altered gait/running patterns, and vice versa, were only a single 'cardio' modality approach used there may be problems in lifting/carrying objects on the surface of Mars. Of course, it should be noted that at present, research is limited and further evidence would likely be required to conclusively suggest a single modality as being sufficient. Further, the suggested approaches mentioned specifically for application of resistance training have not been examined in direct comparison to 'cardio' based modalities. There is scope for this research to be conducted and we feel should be encouraged for future μG analogs such as bed rest studies. In most of the studies cited above though, maximal or near-maximal efforts were employed and in many cases novel resistance training techniques were compared to traditional free weight based resistance training. In combination with the similar positive results between different resistance training approaches when effort is matched, along with the emerging evidence suggesting 'cardio' and resistance training modalities may produce similar adaptations if effort is matched, we pose the hypothesis that adaptations to exercise-induced loading may be more influenced by the manner in which they are performed, primarily the effort put forth, as opposed to the nature of the specific modality utilized. This may result from the similar physiological stimulus experienced when effort is matched. Indeed, as noted effort may be intrinsically linked to motor unit recruitment for performance of physical tasks. However, it should be noted that some work has suggested that, at least at very low efforts (i.e. postural support from m. soleus and m. gastrocnemius during 'dry immersion' involving <7% of maximal voluntary force) motor unit recruitment order may be altered with μG exposure (Shigueva et al., 2015). Whether this would be the case under higher effort exercise conditions in μG is less clear. As such, though we feel there is considerable scope for lessons

Post-print article published on 10/09/2019 (doi: 10.3389/fphys.2019.01150) – all authors confirm they are happy to share this work

learned from traditional terrestrial exercise science studies about effort-based paradigms for exercise-induced skeletal muscle loading to be applied to μG analogs and environments, there remains the need to examine the effects of them both acutely and chronically in these settings.

We reiterate here that resistance training and 'cardio' training do not reflect the entirety of possible approaches to exercise countermeasures, nor are cardiorespiratory fitness, strength, power, and muscle size the only outcomes that might be of interest when discussing the deconditioning that occurs in response to μG environments. However, this review presents emerging evidence from terrestrial setting that, where effort and duration are matched, both resistance training and 'cardio' training may produce largely similar physiological responses and adaptations. These recent advances in understanding of exercise response from terrestrial studies should be considered as candidates for further research within μG analogs and for a wider range of outcome measures as a step towards their consideration for implementation into true μG settings.

References

1. Acheson KJ, Décombaz J, Piquet-Welsch C, Montigon F, Descarli B, Bartholdi I, Fern EB. Energy, protein, and substrate metabolism in simulated microgravity. Am J Physiol. 1995;269(2):R252-260
2. Ahtiainen JP, Hulmi JJ, Kraemer WJ, et al. Strength, endurance or combined training elicit diverse skeletal muscle myosin heavy chain isoform proportion but unaltered androgen receptor concentration in older men. Int J Sports Med. 2009;30(12):879–87.
3. Álvarez C, Ramirez-Campillo R, Ramirez-Vèlez R, Izquierdo M. Effects and prevalence of nonresponders after 12 weeks of high-intensity interval of resistance training in women with insulin resistance: a randomized trial. J Apply Physiol. 2017;122(4):985-996
4. Androulakis-Korakakis P, Langdown L, Lewis A, Fisher JP, Gentil P, Paoli A, Steele J. Effects of exercise modality during additional "high-intensity interval training" on aerobic fitness and strength in powerlifting and strongman athletes. J Strength Cond Res. 2018;32(2):450-457

5. Aniceto RR, Ritti-Dias RM, Scott CB, de Lima FM, dos Prazaeres TMP, do Prado WL. Acute effects of different weight training methods on energy expenditure in trained men. Rev Bras Med Esporte. 2013;19(3):181-185
6. Ashton RE, Tew GA, Aning JJ, Gilbert SE, Lewis L, Saxton JM. Effect of short-term, medium-term, and long-term resistance exercise training on cardiometabolic health outcomes in adults: a systematic review with meta-analysis. Br J Sports Med. 2018; Epub ahead of print.
7. Barcelos LC, Nunes PR, de Souza LR, de Oliviera AA, Furlanetto R, Marocolo M, Orsatti FL. Low-load resistance training promotes muscular adaptation regardless of vascular occlusion, load, or volume. Eur J Apply Physiol. 2015;115(7):1559-1568
8. Behringer M, Schüren T, McCourt M, Mester J. Efficacy of manual versus free-weight training to improve maximal strength and performance for microgravity conditions. J Sports Sci. 2016;34(7):630-636
9. Bloomberg JJ, Peters BT, Cohen HS, Mulavara AP. Enhancing astronaut performance using sensorimotor adaptability training. Front Sys Neurosci. 2015;9:129
10. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. *Introduction to Meta-Analysis.* John Wiley & Sons Ltd, 2009
11. Carlson L, Jonker B, Westcott WL, Steele J, Fisher J. Neither repetition duration, nor number of muscle actions affect strength increases, body composition, muscle size or factes blood glucose in trained males and females. Apply Physiol Nutr Metab. 2018; Epub ahead of print
12. Carpinelli R. Exercise countermeasure to weightlessness during manned spaceflight. Med Sport. 2014;18:42-44
13. Cohen J. *Statistical power analysis for the behavioural sciences.* Hillsdale, N.J.: L. Erlbaum Associates. 1988
14. Cotter JA, Yu A, Haddad F, Kreitenberg A, Baker MJ, Tesch PA, Baldwin KM, Caiozzo VJ, Adams GR. Concurrent exercise on a gravity-independent device during simulated microgravity. Med Sci Sports Exerc. 2015;47(5):990-1000

Post-print article published on 10/09/2019 (doi: 10.3389/fphys.2019.01150) – all authors confirm they are happy to share this work

15. Counts BR, Buckner SL, Dankel SJ, Jessee MB, Mattocks KT, Mouser JG, Laurentino GC, Loenneke JP. The acute and chronic effects of "NO LOAD" resistance training. Physiol Behav. 2016;164:345-352
16. Cromwell RL, Scott JM, Downs M, Yarbough PO, Zanello SB, Ploutz-Snyder L. Overview of the NASA 70-day bed rest study. Med Sci Sports Exercise. 2018;50(9):1909-1919
17. Dankel SJ, Loenneke JP. Effect sizes for paired data should use the change score variability rather than the pre-test variability. J Strength Cond Res. 2018; Epub ahead of print.
18. Davies T, Orr R, Halaki M, Hackett D. Effect of training leading to repetition failure on muscular strength: A systematic review and meta-analysis. Sports Med. 2016;46(4):487-502
19. de Morree HM, Klein C, Marcora S. Perception of effort reflects central motor command during movement execution. Psychophysiology. 2012;49(9):1242-1253
20. Dillon EL, Sheffield-Moore M, Durham WJ, Ploutz-Snyder LL, Ryder JW,, Danesi CP, Randolph KM, Gilkison CR, Urban RJ. Efficacy of testosterone plus NASA exercise countermeasures during head-down bed rest. Med Sci Sports Exercise. 2018;50(9):1929-1939
21. Dorgo S, King GA, Rice CA. The effects of manual resistance training on improving muscular strength and endurance. J Strength Cond Res. 2009;23(1):293-303
22. Duchateau J, Hainaut K. Isometrci or dynamic training: differential effects on mechanical properties of a human muscle. J Apply Physiol Respir Environ Exerc Physiol. 1984;56(2):296-301
23. Enoka RM, Duchateau J. Inappropriate interpretation of surface EMG signals and muscle fiber characteristics impedes understanding of the control of neuromuscular function. J Appl Physiol. 2015;119(12):1516-1518
24. Farup J, de Paoli F, Bjerg K, Rijs S, Ringgard S, Vissing K. Blood flow restricted and traditional resistance training performed to fatigue produce equal muscle hypertrophy. Scand j Med Sci Sports. 2015;25(6):754-763
25. Ferrara CM, Goldberg AP, Ortmeyer HK, et al. Effects of aerobic and resistive exercise training on glucose disposal and skeletal muscle metabolism in older men. J Gerontol A Biol Sci Med Sci. 2006;61(5):480–7.

Post-print article published on 10/09/2019 (doi: 10.3389/fphys.2019.01150) – all authors confirm they are happy to share this work

26. Fisher J, Steele J, Smith D. High- and low-load resistance training: Interpretation and practical application of current research findings. Sports Med. 2017;47(3):393-400
27. Fisher J, Steele J. Questioning the resistance/aerobic training dichotomy: A commentary on physiological adaptations determined by effort rather than exercise modality. J Hum Kinet. 2014;44:137-142
28. Fisher JP, Carlson J, Steele J, Smith D. The effects of pre-exhaustion, exercise order, and rest intervals in a full-body resistance training intervention. Appl Physiol Nutr Metab. 2014;39(11):1265-1270
29. Fisher JP, Carlson L, Steele J. The effects of breakdown set resistance training on muscular performance and body composition in young men and women. J Strength Cond Res. 2016;30(5):1425-1432
30. Fisher JP, Carlson L, Steele J. The effects of muscle action, repetition duration, and loading strategies of a whole-body, progressive resistance training programme on muscular performance and body composition in trained males and females. Apply Physiol Nutr Metab. 2016;41(10):1064-1070
31. Fomina EV, Lysova NY, Chernova MV, Khustnudinova DR, Kozlovskaya IB. Comparative analysis of preventive efficacy of different modes of locomotor training in space flight. Hum Physiol. 2016;42(5):539-545
32. Garma T, Kobayashi C, Haddad F, Adams GR, Bodell PW, Baldwin KM. Similar acute molecular responses to equivalent volumes of isometric, lengthening, or shortening mode resistance exercise. J Appl Physol. 2007;102(1):135-143
33. Gentil P, Bottaro M, Noll M, Werner S, Vasconcelos JC, Seffrin A, Campos MH. Muscle activation during resistance training with no external load – effects of training status, movement velocity, dominance, and visual feedback. Physiol Behav. 2017;179:148-152
34. Gil-Sotomayor A, Williden M, Zinn C, Borotkanics R, Plank L, Kilding A, Harris N. The effect of high intensity interval training or resistance training, both with low-carbohydrate high-fat nutrition on fitness and fat loss in low-active overweight adults. In: Abstract book for the ISBNPA 2018 Annual Meeting in Hong Kong, China, June 3-6

35. Goldberg L, Elliot DL, Keuhl KS. A comparison of the cardiovascular effects of running and weight training. J Strength Cond Res. 1994;8:219-224

36. Grassi B. Bed rest studies as analogs of conditions encountered in space and in diseases. Med Sci Sports Exercise 2018:50(9);1907

37. Grgic J, McIlvenna LC, Fyfe JL, Sabol F, Bishop DJ, Schoenfeld BJ, Pedisc Z. Does aerobic training promote the same skeletal muscle hypertrophy as resistance training? A systematic review and meta-analysis. Sports Med. 2018; Epub ahead of print.

38. Guo F, Sun YJ, Zhang RH. Perceived exertion during muscle fatigue as reflected in movement-related cortical potentials: an event-related potential study. Neuroreport. 2017; 28(3):115-122

39. Hackett DA, Davies TB, Orr R, Kuang K, Halaki M. Effect of movement velocity during resistance training on muscle-specific hypertrophy: A systematic review. Eur J Sport Sci. 2018;18(4):473-482

40. Haddad F, Adams GR, Bodell PW, Baldwin KM. Isometric exercise fails to counteract skeletal muscle atrophy processes during the initial stages of unloading. J Apply Physiol. 2006;100(2):433-441

41. Hepple RT, Mackinnon SL, Goodman JM, Thomas SG, Plyley MJ. Resistance and aerobic training in older men: effects on VO2peak and the capillary supple to skeletal muscle. J Apply Physiol. 1997;82(4):1305-1310

42. Konopka AR, Harber MP. Skeletal muscle hypertrophy after aerobic exercise training. Exerc Sport Sci Rev. 2014;42(2):53-61

43. Kozlovskaya IB, Grigoriev AI, Stepantzov VI. Countermeasure of the negative effects of weightlessness on physical systems in long-term space flights. Acta Astronaut. 1995;36(8-12):661-668

44. Kozlovskaya IB, Grigoriev AI. Russian system of countermeasures on board of the International Space Station (ISS): the first results. Acta Astronaut. 2004;55(3-9):233-237

45. Kozlovskaya IB, Yarmanova EN, Yegorov AD, Stepantsov VI, Fomina EV, Tomilovaskaya ES. Russian countermeasure system for adverse effects of microgravity on long-duration ISS flights. Aerosp Med Hum Perform. 2015;86(12 Suppl):A24-A31

46. Kuznetsov SY, Popov DV, Borovik AS, Vinogradova OL. Wavelet analysis of the m. vastus lateralis surface electromyogram activity in incremental tests until exhaustion using bicycle and knee extension exercises. Hum Physiol. 2011;37:629-635
47. Lang TF, LeBlanc AD, Evans HJ, Lu Y. Adaptation of the proximal femur to skeletal reloading after long duration spaceflight. J Bone Moner Res. 2006;21(8):1224-1230
48. Loehr JA, Guilliams ME, Petersen N, Hirsch N, Kawashima S. Physical training for long-duration spaceflight. Aerosp Med Hum Perform. 2015;86(12, Suppl):A14-A23
49. Loenneke JP, Wilson JM, Bemben MG. Potential exercise countermeasures to attenuate skeletal muscle deterioration in space. J Trainol. 2012;1:1-5
50. MacInnis MJ, McGlory C, Gibala MJ, Phillips SM. Investigating skeletal muscle physiology with unilateral exercise models: when one limb is more powerful than two. Appl Physiol Nutr Metab. 2017;42(6):563-570
51. Maeo S, Kaneshisa H. Maximal voluntary co-contraction training may not always be effective for some leg muscles. J Sports Sci Med. 2014;13(1):217-218
52. Maeo S, Yoshitake Y, Takai Y, Fukunaga T, Kaneshisa H. Effect of short-term maximal voluntary co-contraction training on neuromuscular function. Int J Sports Med. 2014;35(2):125-134
53. Maeo S, Yoshitake Y, Takai Y, Fukunaga T, Kaneshisa H. Neuromuscular adaptations following 12-week maximal voluntary co-contraction training. Eur J Appl Physiol. 2014;114(4):663-673
54. Marcora S. Perception of effort during exercise is independent of afferent feedback from skeletal muscles, heart, and lungs. J Appl Physiol. 2009;106(6):2060-2062
55. Messier SP, Dill ME. Alterations in strength and maximal oxygen uptake consequent to nautilus circuit weight training. Res Q Exerc Sport. 1985;56:345-351
56. Moore AD, Lee SC, Stenger MB, Platts SH. Cardiovascular exercise in the U.S. space program: Past, present, and future. Acta Astronaut. 2010;66(7-8):974-988
57. Morris SB. Estimating effect sizes from pretest-postest-control group designs. Organ Res Methods. 2007;11:364

58. Mulavara AP, Peters BT, Miller CA, Kofman IS, Reschke MF, Taylor LC, Lawrence EL, Wood SJ, Laurie SS, Lee SMC, Buxton RE, May-Phillips TR, Stenger MB, Ploutz-Snyder L, Ryder JW, Feiveson AH, Bloomberg JJ. Physiological and functional alterations after spaceflight and bed rest. Med Sci Sports Exercise. 2018;50(9):1961-1980
59. Murach KA, Minchev K, Grosicki GJ, Lavin KM, Perkins RK, Ryder JW, Scott J, Ploutz-Snyder L, Trappe TA, Trappe S. Myocellular responses to concurrent flywheel training during 70 days of bed rest. Med Sci Sports Exercise. 2018;50(9):1950-1960
60. Noble EB, Pilarski JM, Vora HK, Zuniga JM, Malek MH. Log-transformed EMG amplitude-power output relationships: Single-leg knee-extensor versus single-leg cycle ergometry. J Strength Cond Res. 2017; Epub ahead of print
61. Nóbrega SR, Ugrinowitsch C, Pintanel L, Barcelos C, Libardi CA. Effect of resistance training to muscle failure vs. volitional interruption at high- and low-intensities on muscle mass and strength. J Strength Cond Res. 2018;32(1):162-169
62. Ogasawara R, Kobayashi K, Tsutaki A, Lee K, Abe T, Fujita S, Nakazato K, Ishii N. mTOR signalling response to resistance exercise is altered by chronic resistance training and detraining in skeletal muscle. J Apply Physiol. 2013;114(7):934-940
63. Ozaki H, Loenneke JP, Thiebaud RS, Abe T. Cycle training induces muscle hypertrophy and strength gain: strategies and mechanisms. Acta Physiol Hung. 2015;102(1):1-22
64. Ozaki H, Loenneke JP, Thiebaud RS, Abe T. Resistance training induced to VO_2max in young and older subjects. Eur Rev Aging Phy Act. 2013;10(2):107-116
65. Pageaux B. Perception of effort in exercise science: Definition, measurement and perspectives. Eur J Sport Sci. 2016;16(8):885-894
66. Petersen N, Jaekel P, Rosenberger A, et al. Exercise in space: the European Space Agency approach to in-flight exercise countermeasures for long-duration missions on the ISS. Extrem Physiol Med. 2016;5:9
67. Phillips SM, Winett RA. Uncomplicated resistance training and health-related outcomes: Evidence for a public health mandate. Curr Sports Med Rep. 2010;9(4):208-213

Post-print article published on 10/09/2019 (doi: 10.3389/fphys.2019.01150) – all authors confirm they are happy to share this work

68. Platts AH, Merz CN, Barr Y, et al. effects of sex and gender on adaptation to space: cardiovascular alterations. J Womens Health. 2014;23(11):950-955
69. Ploutz-Synder L, Downs M, Goetchius E, Crowell B, English KL, Ploutz-Snyder R, Ryder JW, Dillon EL, Sheffield-Moore M, Scott JM. Exercise training mitigates multisystem deconditioning during bed rest. Med Sci Sports Exercise. 2018;50(9):1920-1928
70. Poehlman ET, Dvorak RV, DeNino WF, et al. Effects of resistance training and endurance training on insulin sensitivity in nonobese, young women: a controlled randomized trial. J Clin Endocrinol Metab. 2000;85(7):2463–8.
71. Potvin JR, Fuglevand AJ. A motor-unit based model of muscle fatigue. PLoS Comput Biol. 2017;13(6):e1005581
72. Sawczyn S, Mischenko V, Moska W, Sawczyn M, Jagiello M, Kuehne T, Kostrewa-Nowak D, Nowak R, Cięszczyk P. Strength and aerobic training in overweight females in Gdansk, Poland. Open Med. 2015;10:152-162
73. Schoenfeld BJ, Grgic J, Ogborn D, Krieger JW. Strength and hypertrophy adaptations between low- vs. high-load resistance training: A systematic review and meta-analysis. J Strength Cond Res. 2017;31(12):3508-3523
74. Schoenfeld BJ, Ogborn DI, Krieger JW. Effect of repetition duration during resistance training on muscle hypertrophy: a systematic review and meta-analysis. Sports Med. 2015;45(4):577-585
75. Scott C, Nelson E, Martin S, Ligotti B. Total energy costs of 3 Tabata-type calisthenic squatting routines: Isometric, isotonic, and jump. Eur J Hum Mov. 2015;35:34-40
76. Scott CB, Earnest CP. Resistance exercise energy expenditure us greater with fatigue as compared to non-fatigue. J Exerc Physiol. 2011;14(1):1-10
77. Scott JM, Martin D, Ploutz-Snyder R, Downs M, Dillon EL, Sheffield-Moore M, Urban RJ, Ploutz-Snyder L. Efficacy of exercise and testosterone to mitigate atrophic cardiovascular remodelling. Med Sci Sports Exercise. 2018;50(9):1940-1949

78. Scott JPR, Weber T, Green DA. Introduction to the Frontiers Research Topic: Optimization of exercise countermeasures for human space flight – lessons from terrestrial physiology and operational considerations. Frontie Physiol. 2019; doi.org/10.3389/fphys.2019.00173

79. Shiqueva TA, Zakirova AZ, Tomilovskaya ES, Kozlovskaya IB. Effect of support deprivation on the order of motor unit recruitment. Hum Physiol. 2015;41(7):813-816

80. Sillanpaa E, Hakkinen A, Nyman K, et al. Body composition and fitness during strength and/or endurance training in older men. Med Sci Sports Exerc. 2008;40(5):950–8.

81. Silva MH, de Lira CAB, Steele J, Fisher JP, Mota JF, Gomez AC, Gentil P. Effort and duration matched 'High Intensity Interval Training' using cycle ergometry compared to leg press resistance training. SportRχiv. Available at https://osf.io/preprints/sportrxiv/gkxaf

82. Souza D, Barbalho M, Vieira CA, Martins W, Cadore E, Gentil P. Minimal dose resistance training with elastic tubes promotes functional and cardiovascular benefits to older women. Ex Gerontol. 2018; In press

83. Steele J, Butler A, Comerford Z, Dyer J, Lloyd N, Ward J, Fisher J, Gentil P, Scott C, Ozaki H. Similar acute physiological responses from effort and duration matched leg press and recumbent cycling tasks. PeerJ. 2018;6:e4403

84. Steele J, Fisher J, Giessing J, Gentil P. Clarity in reporting terminology and definitions of set endpoints in resistance training. Muscle Nerve. 2017;56(3):368-374

85. Steele J, Fisher J, McGuff D, Bruce-Low S, Smith D. Resistance training to momentary muscular failure improves cardiovascular fitness in humans: A review of acute physiological responses and chronic physiological adaptations. J Exerc Physiol. 2012;15(3):53-80

86. Steele J, Fisher J. Effort, discomfort, group III/IV afferents, bioenergetics, and motor unit recruitment. Med Sci Sports Exerc. 2018;50(8):1718

87. Steele J. Intensity; in-ten-si-ty; noun. 1. Often used ambiguously within resistance training. 2. Is it time to drop the term altogether? Br J Sports Med. 2014;48(22):1586-1588

88. Stein TP, Leskiw MJ, Schluter MD, Hoyt RW, Lane HW, Gretebeck RE, LeBlanc AD. Energy expenditure and balance during spaceflight on the space shuttle. Am J Physiol. 1999;276(6):R1739-1748

89. Tayashiki K, Maeo S, Usui S, Miyamoto N, Kenshisa H. Effect of abdominal bracing training on strength and power of trunk and lower limb muscles. Eur J Appl Physiol. 2016;116(9):1703-1713
90. Tesch PA, Berg HE, Bring D, Evans HJ, LeBlanc AD. Effects of 17-day spaceflight on knee extensor muscle function and size. Eur J Appl Physiol. 2005;93:463-468
91. Trappe S, Costill D, Gallagher P, et al. Exercise in space: human skeletal muscle after 6 months aboard the international space station. J Apply Physiol. 2009;106:1159-1168
92. Vigotsky A, Beardsley C, Contreras B, Steele J, Ogborn D, Phillips SM. Greater electromyographic responses do not imply greater motor unit recruitment and 'hypertrophic potential' cannot be inferred. J Strength Cond Res. 2017;31(1):e1-e4
93. Vilaça-Alves J, Freitas NM, Saavedra FJ, Scott CB, Dos Reis, Simão R, Garrido N. Comparison of oxygen uptake during and after execution of resistance exercises performed on ergometers, matched for intensity. J Hum Kinet. 2016;53:179-187
94. Wilkinson SB, Phillips SM, Atherton PJ, et al. Differential effects of resistance and endurance exercise in the fed state on signalling molecule phosphorylation and protein synthesis in human muscle. J Physiol. 2008;586(Pt 15):3701–17.
95. Yarmanova EN, Kozlovskaya IB, Khimoroda NN, Fomina EV. Evolution of Russian microgravity countermeasures. Aerosp Med Hum Perform. 2015;86(Suppl 1):A32-A37