

Assessing the Usefulness of Acute Physiological Responses Following Resistance Exercise: Sensitivity, Magnitude of Change and Time Course of Measures

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J.S.J., P.G.B., K.v.S. and E.C. conceived and designed the study. J.S.J., P.G.B. and S.G. collected the data. J.S.J., P.G.B., S.G. and G.W.D. analysed the blood samples. J.S.J., P.G.B., and E.C. assembled and analysed the data. J.S.J., P.G.B., K.v.S. and E.C. interpreted the data. J.S.J., P.G.B. and E.C. drafted the manuscript. All authors helped to revise and approve the final version of the manuscript.

Abstract

A variety of strategies exist to modulate acute physiological responses following resistance exercise aimed at enhancing recovery and/or adaptation processes. To assess the true impact of these strategies, it is important to know the ability of measures to detect meaningful change. We investigated the sensitivity of measures used to quantify acute physiological responses to resistance exercise and constructed a physiological profile to characterise the magnitude of change and time course of this response. Eight males, accustomed to regular resistance exercise, performed experimental sessions during a 'control week', void of an exercise stimulus. Participants repeated this sequence of experimental sessions the following week, termed the 'exercise week', except they performed a bout of lower-limb resistance exercise following baseline assessments. Assessments were conducted at baseline, 2, 6, 24, 48, 72 and 96 h post-intervention. Based on the signal-to-noise ratio, the most sensitive measures were maximal voluntary isometric contraction, 20m sprint, countermovement jump peak force, rate of force development (100-200ms), muscle soreness, daily analysis of life demands for athletes Part B, limb girth, matrix metalloproteinase-9, interleukin-6, creatine kinase and high sensitivity C-reactive protein with ratios of >1.5 . There were clear changes in these measures following resistance exercise, determined via magnitude-based inferences. These findings highlight measures that can detect real changes in acute physiological responses following resistance exercise in trained individuals. Researchers investigating strategies to manipulate acute physiological responses for recovery and/or adaptation can use these measures, as well as recommended sampling points, to be confident that their interventions are making a worthwhile impact.

Keywords: physiological profile; strength training; recovery; adaptation; muscle damage; inflammation; muscle soreness; muscle function; reliability; magnitude-based inferences

Introduction

Resistance training results in beneficial adaptations such as increased skeletal muscle size (Fry 2004; Schoenfeld et al. 2016) and strength (Kraemer et al. 2002; Peterson et al. 2004), due in part to acute physiological responses (Peake et al. 2015; Schoenfeld 2012). It is widely accepted that key aspects of the acute physiological response (hours and days post-exercise) are a transient reduction in muscle function, increased muscle soreness, increased swelling of the exercised musculature and increases in the appearance of markers of inflammatory processes and oxidative stress as well as intramuscular proteins and enzymes in the blood (Howatson and Van Someren 2008).

Given the deleterious effects of resistance exercise on proximate performance, there has been keen interest to develop strategies to reduce aspects of the acute physiological response in order to enhance recovery processes (Peake et al. 2017). Conversely, recent reports have suggested that increasing the volume of these physiological responses may be desirable for those looking to enhance adaptive responses to exercise (Peake et al. 2015). To assess the true impact of these strategies, researchers need to know the usefulness of measures in order to detect meaningful change and produce suitable conclusions (Buchheit et al. 2012).

The usefulness of a measure is typically underpinned by: the typical error of the measurement (reliability), the magnitude of the change post-exercise compared with the typical error (signal:noise), and the smallest change in the measure that is of importance to researchers and practitioners, otherwise known as the smallest worthwhile change (Pyne et al. 2004). Previous research has demonstrated good reliability for a range of indirect measures (Howatson and Milak 2009; Morton et al. 2005; Nunan et al. 2010; Pyne 2003). However, only one of these studies (Morton et al. 2005) assessed reliability across a timescale that is reflective of that in which the measure is to be used e.g. to characterise the physiological response in the hours and days post-exercise (Atkinson and Nevill 1998). While what is understood to be the classical physiological response to resistance exercise has been reviewed elsewhere (Clarkson and Hubal 2002;

Howatson and Van Someren 2008), in order to be confident that these changes are real and not just due to random error, an understanding of the measures usefulness is important. Without this information, the documented changes in physiological response measures may simply be noise associated with within-subject variation. To appropriately characterise a measures usefulness to detect changes following exercise requires a control condition identical to the experimental condition but void of the exercise stimulus as well as using the same population which was used to quantify reliability of the measures. This information would enable researchers and practitioners to use the most sensitive measures that would show real effects of strategies that aim to manipulate acute physiological responses for the purposes of recovery and/or adaptation in order to deliver worthwhile impact.

The aim of the present study was twofold: (i) to investigate the sensitivity of a variety of indirect measures used to quantify the acute physiological response to resistance exercise, and (ii) to provide a profile to characterise the magnitude of change and time course of this response. Assessments were scheduled to take place across a timescale that captures the profile of post-exercise physiological perturbations among individuals accustomed to resistance exercise to enhance the applicability of the results.

Materials and methods

Participants

Eight resistance-trained males (age 21 ± 3 years, height 1.81 ± 0.08 m, body mass 82.0 ± 8.0 kg, back squat 6 repetition maximum [RM] 1.2 ± 0.2 x body mass) volunteered to take part in the study. Participants were considered to be resistance-trained if they had performed ≥ 3 resistance sessions per week for ≥ 2 years with a minimum of one session per week including exercises that targeted the lower limbs (Buckner et al. 2017). Prior to any experimental procedures, written informed consent was obtained from all individual participants and the study conformed to the latest revision of the Declaration of Helsinki. All participants completed a health screening questionnaire and were excluded from the study if the investigator deemed they were contraindicated to the study procedures. The study was granted ethical approval (application number: 439) by the London Sports Institute Ethics Sub-Committee at Middlesex University.

Experimental design

In a within-subject design, participants initially performed experimental sessions during a 'control week', which was void of an exercise stimulus in order to assess the reliability of a variety of measures across a relevant timescale. The following week, termed the 'exercise week', participants repeated this sequence of experimental sessions at the same time of day with the exception that they performed a bout of resistance exercise following baseline assessments. The exercise week enabled the characterisation of changes in the same measures from the control week following an acute bout of resistance exercise. Participants attended the laboratory on 12 separate occasions (Figure 1). During visit 1, participants were familiarised with all testing procedures as well as the resistance techniques used for the exercise session (back squat, front squat, good mornings, Bulgarian split-squat). Visit 2 consisted of a second familiarisation session in combination with a 6 RM strength assessment. During visit 3, which occurred 96 h following visit 2, participants completed baseline assessments prior to a 'control period' which

consisted of 1 h rest. Participants then repeated the baseline assessments at 2 h, 6 h, 24 h (visit 4), 48 h (visit 5), 72 h (visit 6) and 96 h (visit 7) post the control period. Visit 8 took place 7 days following visit 3 and required participants to repeat the same testing procedures with the addition of a resistance exercise session that took place immediately after the baseline assessments. Visits 9-12 replicated visits 4-7 for post-exercise assessments. Prior to commencing exercise, participants completed a 5 min warm-up on a stationary cycle ergometer at a self-selected intensity (Wattbike, Nottingham, UK).

Participants were instructed to maintain their habitual diet throughout the study and were asked to record their nutritional intake from visits 3 to 7 and then repeat this from visits 8 to 12. Participants were required to avoid the following throughout the study: exercise external to the protocol, any therapeutic interventions or nutritional supplements, alcohol, caffeine, and non-steroidal anti-inflammatory drugs. Additionally, participants were asked to refrain from food consumption in the two hours prior to any testing procedures.

Strength Assessment

Strength assessments were performed using a 6 RM testing protocol in accordance with recognised guidelines (Haff and Triplett 2015). As part of the warm-up, participants performed three sets of six repetitions of back squat with a progressively increasing load that corresponded to 50, 75, and 90% of their perceived 6 RM. Participants then performed sets of six repetitions with an increasing load for the determination of 6 RM with 2 min rest afforded between attempts and 3 min between exercises. All 6 RM determinations were made within four attempts which were deemed successful by an investigator if a participant had reached a position in which the thigh was at least parallel to the floor. Participants repeated the above procedure for the determination of 6 RM on the front squat, good mornings and Bulgarian split-squat exercises with successful attempts determined by an investigator against standardised techniques. The good morning required participants to place the bar on the upper trapezius with feet slightly wider than shoulder width apart, before bending forwards at the hip until the torso was

parallel to the floor, pausing and then returning to the erect position (Kraemer et al. 1982). During the Bulgarian split-squat participants placed the top of the toes of the trail leg on a 12 inch platform (McCurdy et al. 2010). The lead leg was placed approximately 39-45 inches from the front edge of the platform supporting the trail leg. Participants were then required to squat to a depth where the thigh of the lead leg was parallel to the ground before returning to the start position. These exercises were chosen to target a range of lower limb musculature and are commonly included in strength and conditioning programmes (Haff and Triplett 2015). All resistance exercises were performed using free weights and a standard 20 kg bar (ELEIKO SPORT, Illinois, USA).

Resistance exercise session

As part of the warm-up, participants performed three sets of six repetitions of back squat with a load that corresponded to 50, 75 and 90% of 6 RM. Participants then performed four sets of six repetitions with a load corresponding to 6 RM for the following exercises: back squat, front squat, good mornings and Bulgarian split-squat. The intensity (100% 6 RM or ~85% 1 RM) and volume (12 sets targeting the quadriceps muscle group) of the session were selected based upon recommendations that loads of 80-95% 1 RM elicit maximal gains in strength (Peterson et al. 2005), and hypertrophy (Fry 2004). The performance of at least 8-10 weekly sets per muscle group has also been suggested to be required to maximise increases in muscle strength (Peterson et al. 2005) and size (Schoenfeld et al. 2016) in trained individuals. Participants were instructed to perform the eccentric phase of the exercises in a controlled fashion lasting approximately two seconds, whilst the concentric phase was to be performed with maximal acceleration. This method of lifting was chosen given the suggestion that it is the intended rather than the actual velocity that determines the velocity-specific training response (Behm and Sale 1993). Two minutes rest was afforded between sets and exercises, which has been recommended as a minimum for maximising gains in muscle size (Schoenfeld et al. 2015). If a participant was unable to perform six repetitions of the prescribed load with correct technique (as determined by an investigator), a self-selected reduced load was chosen such that six repetitions could be maintained per set. The volume

load (sets x repetitions x kg) of the session was 6960 ± 903 kg and the training intensity (volume load/total repetitions) was 73 ± 9 kg.

Maximal voluntary isometric contraction

Participants were seated on the dynamometer chair (Humac Norm, CSMi, Massachusetts, USA) with a hip joint angle of 90° and a knee joint angle of 70° (Eddens et al. 2017), set by the investigator using a goniometer. A knee joint angle of 70° has been shown to be sensitive to detect reduced muscle function following eccentric exercise, with no difference between this angle and the torque produced at 90° (McHugh and Tetro 2003). Participants completed a standardised warm-up consisting of efforts at 50, 75 and 90% of perceived maximal force. Participants then performed three maximal voluntary isometric contractions (MVIC) of the dominant limb, each lasting 3 sec, and were asked to contract “as hard and as fast as possible”. Sixty seconds rest was afforded between attempts with peak force (N) recorded and the best attempt used for subsequent analysis.

Countermovement jump

Participants were instructed to stand with their feet shoulder width apart on a force plate (AccuPower, AMTI, Massachusetts, USA) (Walsh et al. 2006), with hands placed on hips. A standardised warm-up was performed consisting of countermovement jumps (CMJ) at 50, 75 and 90% of perceived maximum jump height. Participants then performed three maximal countermovement jumps and were instructed to maximise jump height by using their own choice of depth and pace, whilst maintaining hands on hips throughout and to land with straight legs. Prior to each attempt, the participant prepared themselves in the ready position and motionless on the force plate for at least 1 second to obtain bodyweight and the baseline period. Initiation of the contraction was identified as the first force value less than 5 SD of the baseline period (Chavda et al. 2018). If flight time was exaggerated by participants removing hands from the hips or bending their legs whilst in the air, the test was ordered to be performed again. Sixty seconds rest was afforded between attempts. The sample frequency for data collection was 400 Hz and variables

were calculated using a published spreadsheet (Chavda et al. 2018), with jump height (cm) recorded and the best attempt used for subsequent analysis. Additionally, peak force (CMJ_{PF}) and rate of force development (RFD) were reported for the best attempt and RFD was calculated as the change in force ($N \cdot s^{-1}$) following the onset of the ascent phase of the CMJ in the time intervals 0-50 ms (RFD₀₋₅₀), 0-100 ms (RFD₀₋₁₀₀), 0-200 ms (RFD₀₋₂₀₀), 50-100 ms (RFD₅₀₋₁₀₀) and 100-200 ms (RFD₁₀₀₋₂₀₀). Previous research has reported RFD to differentiate the mechanisms of force loss following eccentric actions depending on the time window studied (Peñailillo et al. 2015) and may be a more sensitive indicator of neuromuscular changes than MVIC force (Maffiuletti et al. 2016). While the rate at which force is developed is also dependent upon the type of muscle action (Tillin et al. 2012).

20 m sprint

Following a warm-up with 20 m runs at 50, 75 and 90% of perceived maximal speed, participants performed three maximal 20 m sprints from a crouched sprinting position, starting 0.3 m behind the start line and leading with the same starting leg for all attempts. Sixty seconds rest was provided between each attempt which were timed using infrared timing gates (Smartspeed, Fusion Sport, Manchester, UK).

Active muscle soreness

Active muscle soreness was determined using a 200 mm visual analogue scale (VAS) with “no pain” indicated at one end and “pain/soreness as bad as it could be” at the other (Bell et al. 2014). Participants were instructed to stand with hands on hips and feet shoulder width apart prior to performing a squat to a depth whereby the thigh was parallel to the floor. Upon completion, participants indicated the pain felt in the lower limbs by drawing a line on the VAS, which was converted to a percentage of the total line for subsequent analysis (Hopkins 2013).

Daily Analysis of Life Demands for Athletes questionnaire

At each time point throughout the study, participants completed the Daily Analysis of Life Demands for Athletes (DALDA) questionnaire (Rushall 1990). The DALDA is divided into parts A and B, which represent the sources of stress and the manifestation of this stress in the form of symptoms, respectively. Part B was used for subsequent analysis based upon previous research showing this aspect was sensitive to determine fatigue and recovery during a period of intensified training (Coutts et al. 2007).

Limb girth

The girth of the dominant limb was measured at the mid-point on the thigh using a flexible anthropometric tape while the participant stood relaxed in the anatomical zero position. Mid-point on the thigh was determined as the halfway point between the anterior superior iliac spine and the proximal aspect of the patella (MacDonald et al. 2014). The mid-point was marked to ensure consistent measurements during subsequent testing procedures. The mean of three measurements was used for subsequent analysis and intra-rater reliability was 0.29%.

Range of motion

Range of motion (ROM) was determined as the difference between the joint angles of maximal voluntary flexion and extension of the knee joint (Chen et al. 2011). Standing in a position of anatomical zero, participants were instructed to elevate and straighten their leg as much as possible at which point the investigator measured the maximally extended angle using a goniometer (EZ Read Jamar Goniometer, Patterson Medical, Illinois, USA). Participants were then instructed to try and touch the hip with the heel whilst maintaining a position where both knees were held together. The investigator measured the maximally flexed angle and recorded this as ROM. All assessments were performed on the dominant limb with the non-dominant limb being used to stabilise the position. The mean of three measurements was used for subsequent analysis and intra-rater reliability was 2.4%.

Sleep Analysis

Participants wore wristwatch actigraphy monitors (wGT3X-BT Monitor, ActiGraph, LLC, FL, USA) to objectively assess sleep parameters alongside self-report sleep diaries. Participants were administered with the monitors following the baseline session and returned the devices following the 96 h session, therefore totalling four 24 h collection periods. The monitor was set to record physical activity using a three-dimensional accelerometer at a sampling rate of 30 Hz which was stored in 1 min epochs. Participants were required to wear the actigraphy monitors on the non-dominant wrist and were instructed to wear the device at all times throughout the study period, except when showering. The self-report sleep diary required participants to record sleep start and end times for each sleep period which were used to determine the start and end of the period analysed (Halson et al. 2014). All sleep periods (including naps) were summed to give total sleep for a 24 h period which was used for subsequent analysis (ActiLife Data Analysis Software, Version 6.11.6, ActiGraph, LLC, FL, USA). The estimation of sleep/wake duration from the actigraphy monitors was determined using a process reported elsewhere (Sargent et al. 2016). The following measures were subsequently calculated, which have been reported to show good agreement with polysomnography when analysed from actigraphy monitors (Sargent et al. 2016):

- Total sleep time (min): the sum of all periods classified as sleep in a given 24 h.
- Wake After Sleep Onset (WASO) (min): the sum of all periods classified as wake between the self-report start and end sleep times.
- Sleep efficiency (%): the percentage of time in bed that was spent asleep.
- Sleep latency (min): the difference between sleep onset time (determined by the ActiLife Data Analysis Software) and sleep start time (defined by participant self-report diary).

Additionally, participants were required to record a subjective rating for each sleep period on a 10-point Likert scale, with 1 being ‘worst possible sleep’ and 10 being ‘best possible sleep’, adapted from previous research (Lastella et al. 2015).

Blood sample collection and analysis

Venous blood samples were collected using the venepuncture technique from a vein in the ante-cubital fossa region by a trained phlebotomist. Blood was collected into two 5 mL serum separator tubes (SST) and two 2.5 mL di-potassium ethylene diamine tetra-acetic acid (EDTA) tubes. Tubes were left to clot for 5 min prior to being centrifuged at 4000 g, 23 °C for 3 min and 2300 g, 23 °C for 10 min for the SST and EDTA tubes, respectively. The serum/plasma was then removed and immediately stored in aliquots at -80 °C for later analysis. Blood samples were analysed for markers of: muscle cell disruption (skeletal troponin I fast form [sTnI], creatine kinase [CK]), inflammatory processes (interleukin-6 [IL-6], interleukin-10 [IL-10], high-sensitivity c-reactive protein [hsCRP], matrix metalloproteinase-9 [MMP-9]), and oxidative stress (protein carbonyls [PC], lipid hydroperoxides [LOOH], ascorbyl free radical). The time of collection for all blood markers was based upon likely known time-course responses (Table 1) and the intra and inter-assay coefficient of variation is presented in Table 2.

Serum sTnI (Elabscience, Maryland, USA), IL-6, MMP-9 (Invitrogen Corporation, California, USA), IL-10 (Thermo Scientific, Maryland, USA) and hsCRP (R&D Systems, Inc., Minnesota, USA) were determined by an enzyme-linked immunosorbent assay (ELISA) using commercially available kits.

Serum CK was determined using a CK NAC-activated kit (Randox Laboratories Ltd, County Antrim, UK). Ten μL of sample was mixed with 500 μL reagent and absorbance was read at 37 °C on an Rx Monza clinical chemistry analyser (Randox Laboratories Ltd, County Antrim, UK).

Serum PC samples were initially tested for their protein concentration using a Bradford Assay (Pierce™ Coomassie; Thermo Scientific, Maryland, USA). The results of which demonstrated that samples required a dilution factor of 1:5000 to fall within the recommended 10 $\mu\text{g}/\text{mL}$ range for determination of PC using a commercially available ELISA kit (Oxiselect™; Cell Biolabs, Inc., California, USA).

The ferrous iron/xylenol orange (FOX) assay (Wolff 1994) was used to quantify the susceptibility to iron-induced LOOH formation in blood, as a measure of exercise-induced lipid peroxidation. Given the presence of iron ions in the assay protocol, higher LOOH values may be reported compared to other

methods (Clifford et al. 2016). Absorbance was read at 560 nm using a spectrophotometer (U-2001, Hitachi, Berkshire, UK) (range 0-5 $\mu\text{mol}\cdot\text{L}^{-1}$).

Electron paramagnetic resonance (EPR) spectroscopy was used to quantify the formation of ascorbyl free radical in blood using a Bruker EMX series X-band EPR spectrophotometer (Bruker, Karlsruhe, Germany). Briefly, 1 mL plasma and 1 mL dimethyl sulfoxide (DMSO) were mixed and slowly flushed into an aqua X multiple bore cavity cell. The EMX parameter settings were as follows; frequency, 9.785 GHz; microwave power, 20 mW; modulation frequency, 100 kHz; and modulation amplitude, 1.194 G. All EPR spectra underwent 3 scans, which were subsequently analysed, following the application of an 11-point filter, using WinEPR software (Version 3.2, Bruker WinEPR, Coventry, UK). The average spectral peak-to-trough line amplitude was used to determine free radical concentration.

Statistical analysis

Reliability and signal-to-noise-ratio

Typical error was calculated for reliability (Hopkins 2000) during the control week and presented as coefficient of variation (%) using a published spreadsheet (Hopkins 2015). Range of motion, DALDA and sleep rating values are presented as absolute values. Signal-to-noise ratio refers to the magnitude of the largest mean effect observed between the exercise week and control week at any time point, divided by the typical error calculated from the control week (Buchheit 2014).

Magnitude of change and time course of the acute physiological response

Measures with a signal-to-noise ratio of greater than 1.5 were then analysed by making probabilistic magnitude-based inferences about the observed magnitude of the effect between the control and exercise weeks to assess the likelihood that changes are real using the methods described by Batterham and Hopkins (2006). A change greater than 1.5 times the typical error was selected as the threshold based upon the suggestion that this can be considered a real change as opposed to noise associated with within-

subject variation (Hopkins 2000). Magnitude-based inferences build on the signal-to-noise ratio as this method takes into account the individual responses, as demonstrated by the confidence intervals, as well as the smallest worthwhile change before making the final interpretation (Hopkins et al. 2009; Hopkins and Batterham 2016). The smallest worthwhile change was standardised as a fraction of the between-subject SD at baseline from both the control and exercise weeks using the smallest change in the mean of 0.2 (Batterham and Hopkins 2006). The smallest worthwhile change was used to determine the effect of the independent variable on each dependent variable using a spreadsheet designed for analysis of a crossover trial (Hopkins 2006). Given the large number possible, comparisons were made between baseline and each subsequent time point (i.e. baseline-2 h, baseline-6 h, baseline-24 h, baseline-48 h, baseline-72 h, baseline-96 h) with differences compared between the control and exercise weeks. Mean values of log-transformed data were back-transformed to provide mean percentage change and 90% confidence intervals, with measures that had large percentage changes presented as factors (Hopkins 2003). Values for the DALDA were not log-transformed and are presented as absolute values. Standardised changes of 0.20, 0.60, 1.20, 2.0, and 4.0 were thresholds for small, moderate, large, very large and extremely large effects, respectively (Hopkins et al. 2009). When the confidence interval for a change included both small positive and negative effects, the change was deemed unclear. For clear effects, the qualitative probabilities that the true effect was substantial was defined by the following scale: 25-75% possibly, 75-95% likely, 95-99.5% very likely, >99.5% most likely (Hopkins 2006). Examples of different interpretations from magnitude-based inferences have been described elsewhere (Buchheit 2016). A paired samples t-test was performed to check differences between the baseline values for the control and exercise weeks with mechanistic inferences derived using a published spreadsheet (Hopkins 2017). Where presented, baseline values are reported as the absolute mean \pm SD with all other values reported as the mean effect between the control and exercise weeks; \pm or \times/\div 90% confidence intervals.

Results

Reliability and signal-to-noise ratio

Table 3 shows the typical error and signal-to-noise ratio for all measures. Based on the signal-to-noise ratio, the most sensitive measures were MVIC, 20 m sprint, CMJ_{PF}, RFD₁₀₀₋₂₀₀, muscle soreness, DALDA Part B, limb girth, MMP-9, IL-6, CK, hsCRP and ascorbyl free radical which all had a ratio of >1.5. All of the other measures were therefore not reliable enough or did not change sufficiently post-exercise to be sensitive to detect change in acute physiological responses.

Magnitude of change and time course of the acute physiological response

Baseline values were *likely* greater for the exercise week compared to the control week for MVIC force and CMJ_{PF}, and *likely* smaller for hsCRP. All other effects between baseline values were *unclear*.

Isometric Muscle Function

Baseline values for MVIC force were 242 ± 55 N and 264 ± 60 N for the control and exercise weeks, respectively. There was a *most likely* moderate reduction in maximal muscle function following the resistance exercise session at 2 h post-exercise ($-19.3; \pm 5.7\%$; Figure 2). The decrease in force production was *very likely* moderate at 6 h ($-13.1; \pm 6.1\%$), *most likely* moderate at 24 h ($-12.9; \pm 3.0\%$), *likely* small at 48 h ($-7.8; \pm 7.9\%$) and *possibly* small at 96 h post-exercise ($-6.9; \pm 9.0\%$) compared to the control week. Effects were *unclear* at 72 h post-exercise ($-4.8; \pm 10.8\%$).

20 m Sprint Performance

Baseline 20 m sprint times were 3.15 ± 0.10 s and 3.15 ± 0.06 s for the control and exercise weeks, respectively. An impairment in sprint performance was *very likely*, demonstrated by an increased 20 m sprint time at 2 h (large effect, $4.2; \pm 2.3\%$) and 6 h post-exercise (moderate effect, $3.0; \pm 1.8\%$) as well as *likely* small increases in sprint time at 24 h ($1.6; \pm 2.1\%$) and 48 h post-exercise ($1.1; \pm 1.3\%$)

compared to the control week (Figure 2). There was an *unclear* outcome at 72 h ($0.9; \pm 1.8\%$), while sprint time was *possibly* decreased at 96 h post-exercise (small effect, $-0.8; \pm 1.8\%$).

Countermovement Jump

At baseline, CMJ_{PF} was 1059 ± 103 N and 1212 ± 209 N for the control and exercise weeks, respectively. There was a *most likely* large reduction in force at 2 h ($-19; \pm 6.2\%$) and 6 h ($-20; \pm 6.3\%$), *very likely* large decrease at 24 h ($-20; \pm 11\%$), 48 h ($-19; \pm 9.3\%$) and 72 h ($-20; \pm 14\%$) and *likely* moderate impairment at 96 h post-exercise ($-14; \pm 14\%$).

Rate of Force Development

Baseline values for RFD₁₀₀₋₂₀₀ were 582 ± 243 N·s⁻¹ and 550 ± 315 N·s⁻¹ for the control and exercise weeks, respectively. There was a *likely* small reduction in RFD₁₀₀₋₂₀₀ at 2 h ($-22; \pm 24\%$), *likely* moderate reduction at 24 h ($-34; \pm 24\%$), *very likely* moderate decrease at 48 h ($-46; \pm 25\%$) and a *likely* moderate decrease at 72 h ($-43; \pm 37\%$). Force production was *likely* moderately increased at 96 h ($27; \pm 33\%$), while effects at 6 h were *unclear* ($-0.2; \pm 33\%$).

Limb Girth

Baseline limb girth values were 61 ± 2.6 cm and 61 ± 2.5 cm for the control and exercise weeks, respectively. Effects at 2 h ($0.6; \pm 0.7\%$) and 6 h ($0.4; \pm 0.6\%$) post-exercise were *likely trivial* compared to the control week, respectively (Figure 2). There were *possible* increases in limb girth at 24 h (small effect, $0.9; \pm 0.8\%$), 48 h (small effect, $1.1; \pm 1.1\%$), 72 h ($0.7; \pm 0.8\%$) and 96 h ($0.8; \pm 0.7\%$) post-exercise compared to the control week.

Muscle Soreness

Baseline muscle soreness values were $9.0 \pm 13.0\%$ and $4.6 \pm 4.4\%$ for the control and exercise weeks, respectively. Muscle soreness was *very likely* increased at 2 h (large effect, $6.0; \pm 2.8$), *most likely*

increased at 6 h (large effect, 5.4; $x/\div 2.2$) and 24 h (large effect, 10.3; $x/\div 2.8$), *very likely* increased at 48 h (very large effect, 12.4; $x/\div 5.1$) and 72 h (large effect, 8.4; $x/\div 3.3$), and *likely* increased at 96 h post-exercise (moderate effect, 2.7; $x/\div 2.6$) compared to the control week (Figure 3).

Daily Analysis of Life Demands for Athletes

At baseline, participants reported 2 ± 2 aspects of the DALDA Part B as ‘worse than normal’ during both the control and exercise weeks. There was a *likely* increase in the number of ‘worse than normal’ ratings at 2 h (small effect, 1; ± 1) and 6h (moderate effect, 1; ± 1), *very likely* increase at 24 h (moderate effect, 2; ± 1), and *likely* increase at 48 h (moderate effect, 1; ± 1) and 72 h (small effect, 1; ± 1) post-exercise compared to the control week (Figure 3). There was a *likely* decrease in the number of ‘worse than normal’ ratings at 96 h post-exercise (small effect, -1; ± 1) compared to the control week.

Blood Analysis

Baseline MMP-9 concentrations were $199\ 781 \pm 113\ 892\ \text{pg}\cdot\text{mL}^{-1}$ and $175\ 586 \pm 54\ 072\ \text{pg}\cdot\text{mL}^{-1}$ for the control and exercise weeks, respectively. There was a *very likely* moderate increase in MMP-9 concentrations at 2 h post-exercise ($29.3; \pm 21.4\%$) compared to the control week (Figure 4). Effects were *unclear* at 6 h ($15.3; \pm 39.6\%$), *possibly* decreased at 24 h ($-4.0; \pm 26.6\%$) and *unclear* at 48 h ($-1.9; \pm 27.0\%$), 72 h ($6.5; \pm 29.3\%$) and 96 h post-exercise ($10.6; \pm 31.0\%$).

The concentration of IL-6 was $1.05 \pm 0.44\ \text{pg}\cdot\text{mL}^{-1}$ and $0.95 \pm 0.22\ \text{pg}\cdot\text{mL}^{-1}$ at baseline for the control and exercise weeks, respectively. There was a *very likely* increase in IL-6 at 2 h (moderate effect, 1.51; $x/\div 1.37$) and 6 h post-exercise (very large effect, 2.98; $x/\div 2.39$) compared to the control week (Figure 4). There was a *possible* decrease in IL-6 at 24 h post-exercise ($0.98; x/\div 1.25$) compared to the control week.

Baseline CK concentrations were $408 \pm 707\ \text{U}\cdot\text{L}^{-1}$ and $312 \pm 422\ \text{U}\cdot\text{L}^{-1}$ for the control and exercise weeks, respectively. Exercise resulted in a *very likely* moderate increase in CK concentrations at 24 h ($2.0; x/\div 1.6$) and a *likely* small increase at 48 h ($1.5; x/\div 1.6$) post-exercise compared to the control week

(Figure 4). Effects were *unclear* at 72 h (1.2; $x/\div 1.5$), while there was a *possible* decrease at 96 h post-exercise (0.8; $x/\div 1.7$) compared to the control week.

The concentration of hsCRP was $0.64 \pm 0.55 \text{ mg}\cdot\text{L}^{-1}$ and $0.40 \pm 0.27 \text{ mg}\cdot\text{L}^{-1}$ for the control and exercise weeks, respectively. Concentrations of hsCRP were *very likely* increased at 24 h (small effect, 1.7; $x/\div 1.3$), as well as there being a *likely* small increase at 48 h (1.4; $x/\div 1.5$) and 72 h post-exercise (1.7; $x/\div 1.5$) compared to the control week (Figure 4). Effects were *unclear* at 96 h post-exercise (1.5; $x/\div 1.9$).

Values for ascorbyl free radical were $436\,425 \pm 232\,381 \text{ AU}$ and $400\,094 \pm 199\,382 \text{ AU}$ at baseline for the control and exercise weeks, respectively. There was a *likely trivial* effect of exercise at 2 h post-exercise (1.1; $x/\div 1.3$) compared to the control week. Effects were *unclear* at 6 h (0.9; $x/\div 2.4$), 24 h (0.8; $x/\div 2.2$) and 48 h post-exercise (0.7; $x/\div 2.1$).

Discussion

This study had two primary purposes: (i) to provide information as to the sensitivity of a variety of measures used as indirect measures to quantify the acute physiological response to resistance exercise, and (ii) to provide a profile to characterise the magnitude of change and time course of this response. We quantified these results in individuals accustomed to resistance exercise across a timescale common to research investigating acute physiological responses, allowing transferability of the results. The results of this study indicate that MVIC, 20 m sprint, CMJ_{PF}, RFD₁₀₀₋₂₀₀, muscle soreness, limb girth, DALDA Part B, MMP-9, IL-6, CK, hsCRP and ascorbyl free radical were sensitive measures to detect change in response to resistance exercise, with a signal-to-noise ratio of >1.5 . Using these measures, clear effects were reported with aspects of the acute physiological response apparent as soon as 2 h, through to 96 h post-exercise, determined via magnitude-based inferences.

Reliability and signal-to-noise ratio

Following resistance exercise, muscle soreness was the measure most sensitive to detect change in trained individuals as demonstrated by a signal-to-noise ratio of 15.0. A variety of other measures also showed a signal-to-noise ratio of >1.5 . Previous research using this method to track aerobic training adaptations reported exercise heart rate as the most sensitive measure to change with a signal-to-noise ratio of 1.6 (Buchheit 2014). The measures in the present study therefore compare favourably.

All of the other measures assessed in this study either exhibited poor reliability or did not demonstrate a post-exercise change that was of great enough magnitude to provide a signal-to-noise ratio of >1.5 . Taking LOOH and CK as examples, by just showing the typical error, it may be assumed that LOOH (12%) are a more sensitive marker in this scenario than CK (28%). However, once the magnitude of post-exercise change is considered, it becomes apparent that resistance exercise has a profound impact upon CK (98% increase), whilst LOOH are relatively unchanged (3.5% increase/decrease). Taking both the reliability and magnitude of change post-exercise into account with the signal-to-noise ratio, these results

provide novel information as to the sensitivity for a range of measures used to assess acute physiological responses following resistance exercise.

In the current study, the signal-to-noise ratio was ≤ 1.5 for a range of measures suggesting either significant typical error during the control week, or a lack of change during the exercise week contributed to the outcome that these markers were not sensitive enough to detect changes in acute physiological responses. We report these findings in contrast to others that have shown resistance exercise to impact: jump height (Byrne and Eston 2002a, 2002b) and ROM (Chen et al. 2011), as well as the concentrations of sTnI (Rankin et al. 2015), IL-10 (Hirose et al. 2004) and PC (Bowtell et al. 2011). Interestingly, RFD₁₀₀₋₂₀₀ was the only RFD time point sensitive to change, highlighting that even different aspects of the same measure may exhibit varying levels of usefulness. Differences in our findings compared to previous research may be attributed to either the training status of participants or the level of mechanical challenge imposed by the exercise bout such that these factors negated any impact upon these measures in the present study. Alternatively, these studies may have reported changes that were within the typical error of the measurement. It is noteworthy that our study utilised an exercise session designed to target the lower limbs and the upper body response may be different (Vernillo et al. 2018). The authors acknowledge that it is unfeasible to expect all researchers to conduct reliability studies prior to an investigation. Therefore this study provides information as to the reliability of a range of measures for use in future research, whilst incorporating important facets such as the use of a frequently used cohort and matching the time scale between baseline and follow up assessments (Atkinson and Batterham 2015).

Magnitude of change and time course of the acute physiological response

Resistance exercise impaired MVIC force and 20 m sprint performance which peaked at 2 h post-exercise with the effects still apparent for the ensuing days following the exercise bout. Clear effects on numerous physiological and perceptual measures further highlight the multitude of acute physiological responses. These findings support previous research which demonstrates a similar range of perturbations following

resistance exercise in the hours and days post-exercise (Miles et al. 2008; Vincent and Vincent 1997). In the context of this study, measures such as MVIC/20 m sprint/CMJ_{PF}/RFD₁₀₀₋₂₀₀, MMP-9/IL-6/hsCRP and CK reflect disturbances to muscle function (Morton et al. 2005; Peñailillo et al. 2015), inflammatory processes (Miles et al. 2008; Peake et al. 2005) and muscle cell membrane integrity (Brancaccio et al. 2007; Clarkson and Hubal 2002), respectively.

Increased perceptions of muscle soreness occurred concomitantly with higher 'worse than normal' ratings on the DALDA Part B, suggesting feelings of soreness and stress are an important facet of the acute post-exercise period. Muscle soreness is a well-established physiological response to resistance exercise (Miles et al. 2008; Vincent and Vincent 1997). Here we present novel information that Part B of the DALDA is sensitive to change in the acute period following a single bout of resistance exercise, increasing the potential application of this measure in addition to overtraining research (Coutts et al. 2007). Together our findings highlight sensitive measures that are able to detect changes to characterise the magnitude of change and time course of the acute physiological response to resistance exercise. Table 4 provides the recommended sampling points so that researchers/practitioners can capture meaningful changes in these measures.

Research has demonstrated that strategies designed to attenuate acute physiological responses can accelerate recovery processes (Bowtell et al. 2011; Rankin et al. 2015), whilst others suggest that these disturbances may form part of the normal response required as part of the adaptive process (Peake et al. 2015; Roberts et al. 2015). An understanding of the most sensitive measures as well as recommended sampling points provides key information for those seeking to identify the effectiveness of imposed strategies that look to manipulate acute physiological responses for the purposes of recovery and/or adaptation. Application of these results may also be of benefit for those profiling an individual's readiness to train.

Despite a signal-to-noise ratio of 2.2, the peak effect of resistance exercise on ascorbyl free radical was *unclear*. This may be explained by the significant variation in individual responses, as demonstrated by large confidence intervals, which showed both a substantial increase and decrease in the concentration following the exercise bout. Therefore this may be considered a sensitive measure but would have required greater than eight participants to detect real changes following the resistance exercise bout in this study. However, results calculated in this way may only apply in the context of the selected study (Buchheit 2014). Whether similar findings would be seen in the context of different forms of exercise or in a cohort of untrained individuals remains to be elucidated.

A potential limitation of the study is the difference in baseline values for MVIC force, CMJ_{PF} and hsCRP. It is possible that the baseline measures of the control week may have been impacted by the pre-testing 6 RM strength assessment conducted 96 h prior. However, MVIC force and hsCRP had returned to baseline at 96 h following the exercise intervention, which would be expected to demonstrate a greater response compared to the 6 RM strength assessment, and along with all other measures showing *unclear* effects between baseline values, the likelihood of this is reduced. Instead this perhaps highlights learning effects (performance measures) and biological variation (blood markers) that may exist despite familiarisation and control measures which further highlights the value of our data in providing the typical error of measures across an appropriate timescale.

In summary, present findings show that MVIC force, 20 m sprint performance, CMJ_{PF}, RFD₁₀₀₋₂₀₀, limb girth, muscle soreness, DALDA Part B, MMP-9, IL-6, CK and hsCRP are useful measures to detect meaningful change in acute physiological responses to resistance exercise in trained individuals. When characterising the magnitude of change and time course of this response, the present study identifies recommended sampling points for future research. The application of our data are valuable to researchers and practitioners looking to investigate the effectiveness of strategies that manipulate acute physiological responses in order to optimise recovery processes and/or training adaptation as well as strength and conditioning coaches profiling an individual's readiness to train.

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Table 1. List of blood markers measured at specific time points.

Marker	Baseline	2h	6h	24h	48h	72h	96h
sTnI	✓	✓	✓	✓	✓	✓	✓
MMP-9	✓	✓	✓	✓	✓	✓	✓
IL-6	✓	✓	✓	✓			
IL-10	✓	✓	✓	✓			
CK	✓			✓	✓	✓	✓
hsCRP	✓			✓	✓	✓	✓
PC	✓	✓	✓	✓	✓		
LOOH	✓	✓	✓	✓	✓		
Ascorbyl	✓	✓	✓	✓	✓		

sTnI, skeletal troponin I fast form; MMP-9, matrix metalloproteinase-9; IL-6, interleukin-6; IL-10, interleukin-10; CK, creatine kinase; hsCRP, high sensitivity c-reactive protein; PC, protein carbonyls; LOOH, lipid hydroperoxides; Ascorbyl, ascorbyl free radical.

Table 2. Intra and inter-assay coefficient of variation (%) for markers from the blood analysis.

Marker	Coefficient of variation (%)	
	Intra-assay	Inter-assay
sTnI ¹		<10
MMP-9 ¹	3.3-4.6	6.9-8.0
IL-6 ¹	5.1-7.7	6.5-9.3
IL-10 ¹	<10	<10
CK ¹	2.3	3.9
hsCRP ¹	3.8-8.3	6.0-7.0
PC ²		8
LOOH ³	4.6	6
Ascorbyl		

¹Reported by the kit manufacturer; ²(Bowtell et al. 2011); ³(Davison et al. 2008). sTnI, skeletal troponin I fast form; MMP-9, matrix metalloproteinase-9; IL-6, interleukin-6; IL-10, interleukin-10; CK, creatine kinase; hsCRP, high sensitivity c-reactive protein; PC, protein carbonyls; LOOH, lipid hydroperoxides; Ascorbyl, ascorbyl free radical.

Table 3. Values for the typical error and signal-to-noise ratio for a range of measures.

Measure	Typical Error	Signal-to-noise ratio	ICC
Muscle soreness	72%	15.0	0.66 ± 0.22
20 m sprint	1.1%	3.8	0.92 ± 0.07
MVIC	5.4%	3.6	0.96 ± 0.03
Creatine Kinase	28%	3.5	0.94 ± 0.05
CMJ _{PF}	6.6%	3.1	0.63 ± 0.23
Limb girth	0.5%	2.2	0.99 ± 0.01
Ascorbyl Free Radical	12%	2.2	0.97 ± 0.02
hsCRP	35%	2.0	0.94 ± 0.05
RFD ₁₀₀₋₂₀₀	24%	1.9	0.90 ± 0.07
DALDA Part B	0.9	1.7	0.89 ± 0.08
IL-6	114%	1.7	0.20 ± 0.10
MMP-9	18%	1.6	0.83 ± 0.11
Sleep latency	149%	1.5	N/A
Sleep rating	0.6	1.3	N/A
RFD ₀₋₂₀₀	21%	1.2	0.93 ± 0.05
Jump height	12%	0.8	0.63 ± 0.23
Total sleep time	10%	0.8	N/A
sTnI	34%	0.8	0.80 ± 0.13
RFD ₅₀₋₁₀₀	41%	0.8	0.87 ± 0.09
IL-10	17%	0.7	1.00 ± 0.01
RFD ₀₋₁₀₀	29%	0.7	0.91 ± 0.06
Sleep efficiency	5.4%	0.6	N/A
Protein Carbonyls	21%	0.6	0.83 ± 0.12

Range of motion	2.6°	0.5	0.91 ± 0.06
RFD ₀₋₅₀	59%	0.5	0.71 ± 0.20
WASO	39%	0.4	N/A
Lipid Hydroperoxides	12%	0.3	0.75 ± 0.16

ICC, Intraclass correlation coefficient; MVIC, Maximal Voluntary Isometric Contraction; CMJ_{PF}, countermovement jump peak force; RFD, Rate of Force Development; DALDA, Daily Analysis of Life Demands for Athletes; WASO, Wake After Sleep Onset; sTnI, skeletal troponin fast form; MMP-9, matrix metalloproteinase-9; hsCRP, high sensitivity C-reactive protein; IL-6, interleukin-6; IL-10, interleukin-10. Solid line represents threshold for the signal-to-noise ratio (Buchheit 2014), with measures above the line taken forward for subsequent analysis (Hopkins 2000).

Table 4. Recommended sampling points for measures that exhibited clear effects.

Measure	2h	6h	24h	48h	72h	96h
MVIC	✓*	✓	✓	✓		
20 m sprint	✓*	✓	✓	✓		
CMJ _{PF}	✓	✓*	✓	✓	✓	✓
RFD ₁₀₀₋₂₀₀	✓		✓	✓*	✓	✓
Limb girth			✓	✓*	✓	✓
Muscle soreness	✓	✓	✓	✓*	✓	✓
DALDA Part B	✓	✓	✓*	✓	✓	
Creatine Kinase			✓*	✓		
hsCRP			✓*	✓	✓	
IL-6	✓	✓*				
MMP-9	✓*					

MVIC, Maximal Voluntary Isometric Contraction; CMJ_{PF}, countermovement jump peak force; RFD, rate of force development; DALDA, Daily Analysis of Life Demands for Athletes; hsCRP, high sensitivity C-reactive protein; IL-6, interleukin-6; MMP-9, matrix metalloproteinase-9. * represents the peak change for a given measure.

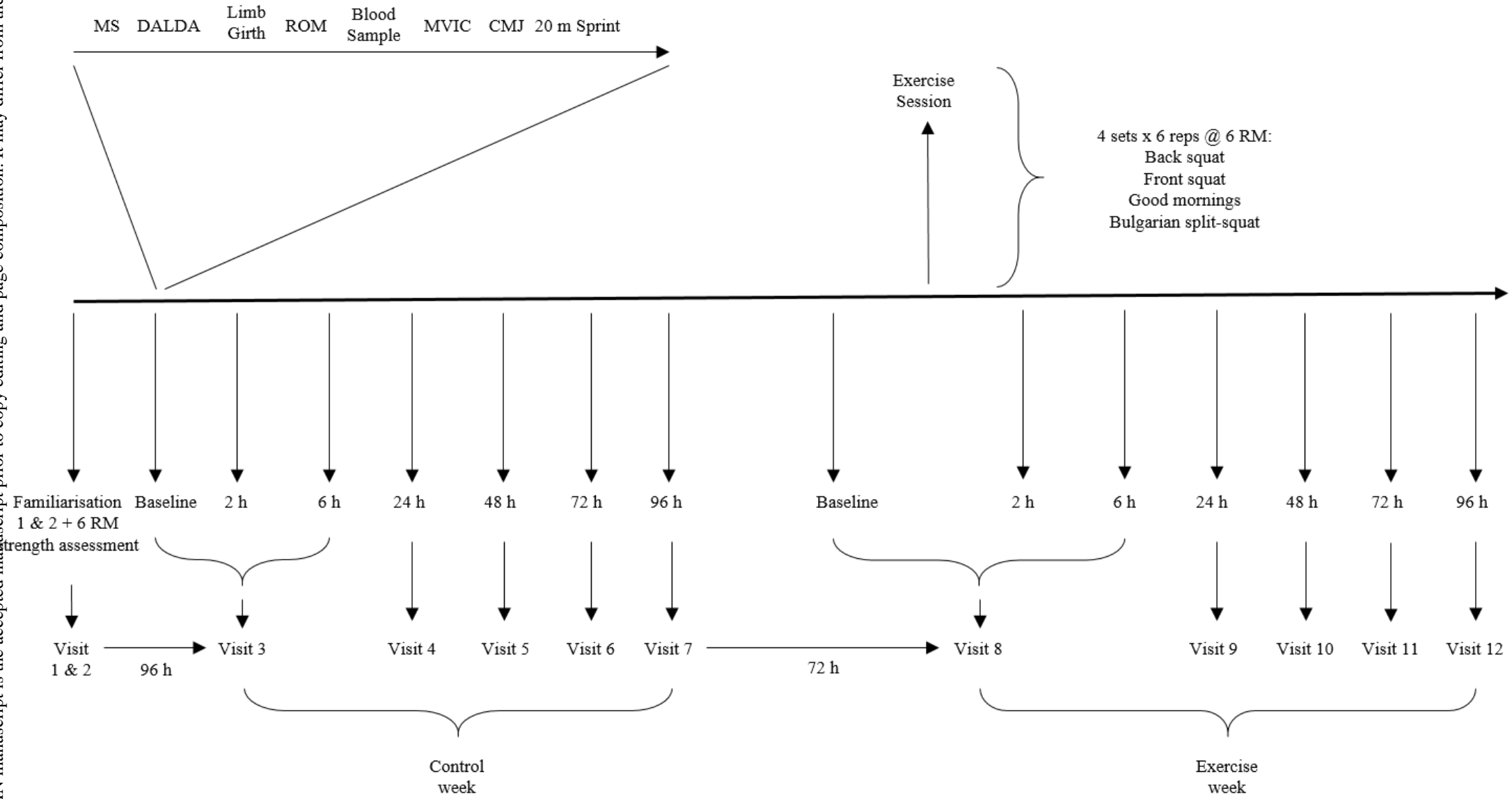
Figure Legends

Fig. 1 Schematic overview of the study timelines. The order of assessments is depicted for the Baseline session of the control week which was replicated for all subsequent time points. MS, muscle soreness; DALDA, daily analysis of life demands for athletes; ROM, range of motion; MVIC, maximal voluntary isometric contraction; CMJ, countermovement jump; RM, repetition maximum

Fig. 2 Percentage change from baseline in (a) maximal voluntary isometric contraction force, (b) 20 m sprint time and (c) limb girth. The shaded area represents the smallest worthwhile change compared with the baseline value. The error bars represent 90% confidence intervals. The number of asterisks (*) indicate the likelihood for the changes to be substantial, with * referring to possible changes, ** to likely, *** to very likely and **** to most likely changes

Fig. 3 Change from baseline in (a) muscle soreness and (b) Daily Analysis of Life Demands for Athletes. The shaded area represents the smallest worthwhile change compared with the baseline value. The error bars represent 90% confidence intervals. The number of asterisks (*) indicate the likelihood for the changes to be substantial, with * referring to possible changes, ** to likely, *** to very likely and **** to most likely changes

Fig. 4 Change from baseline in (a) matrix metalloproteinase-9 (MMP-9), (b) high sensitivity C-reactive protein (hsCRP), (c) interleukin-6 (IL-6) and (d) creatine kinase concentrations. The shaded area represents the smallest worthwhile change compared with the baseline value. The error bars represent 90% confidence intervals. The number of asterisks (*) indicate the likelihood for the changes to be substantial, with * referring to possible changes, ** to likely, *** to very likely and **** to most likely change



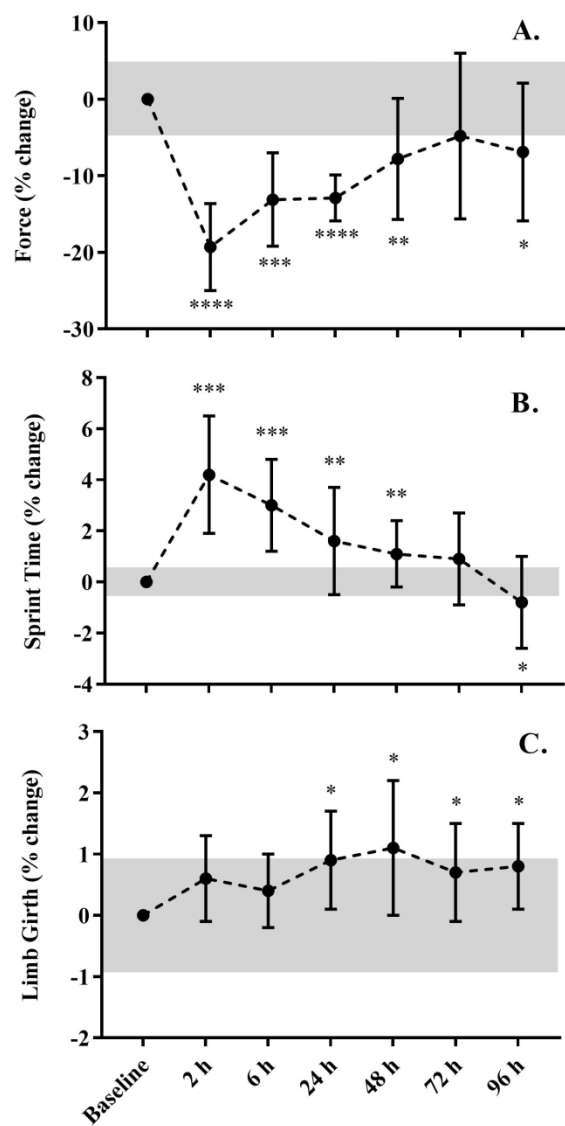


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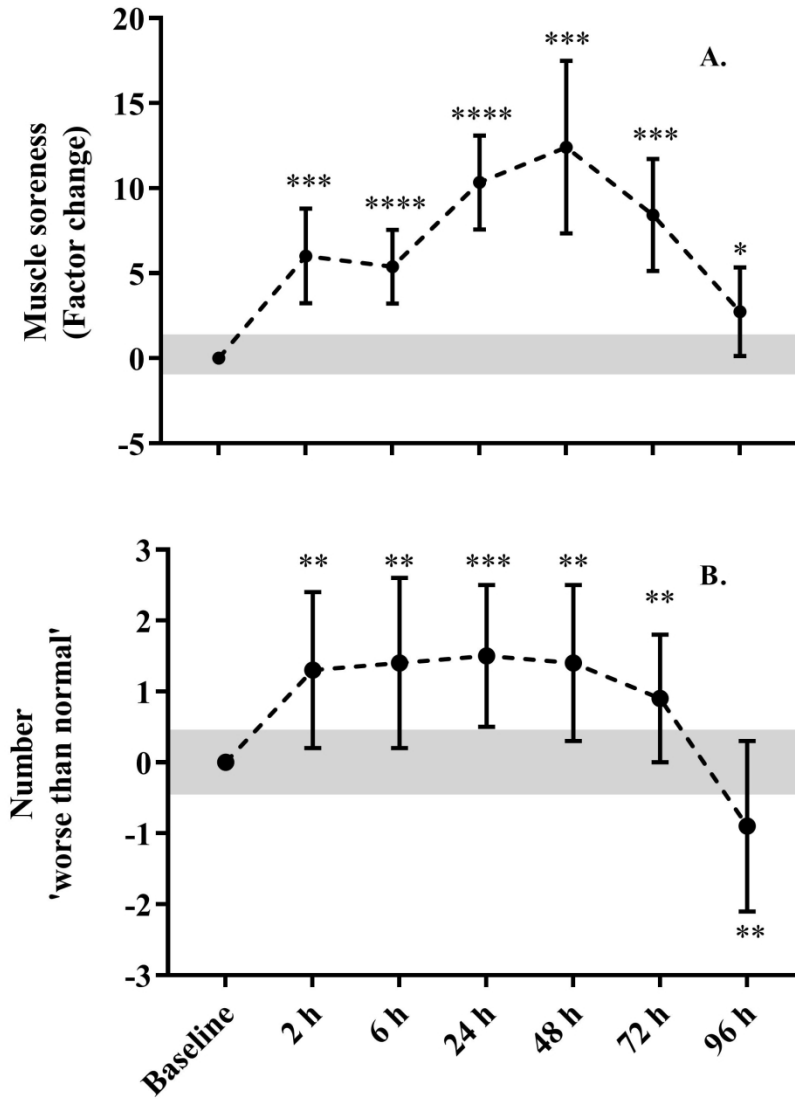


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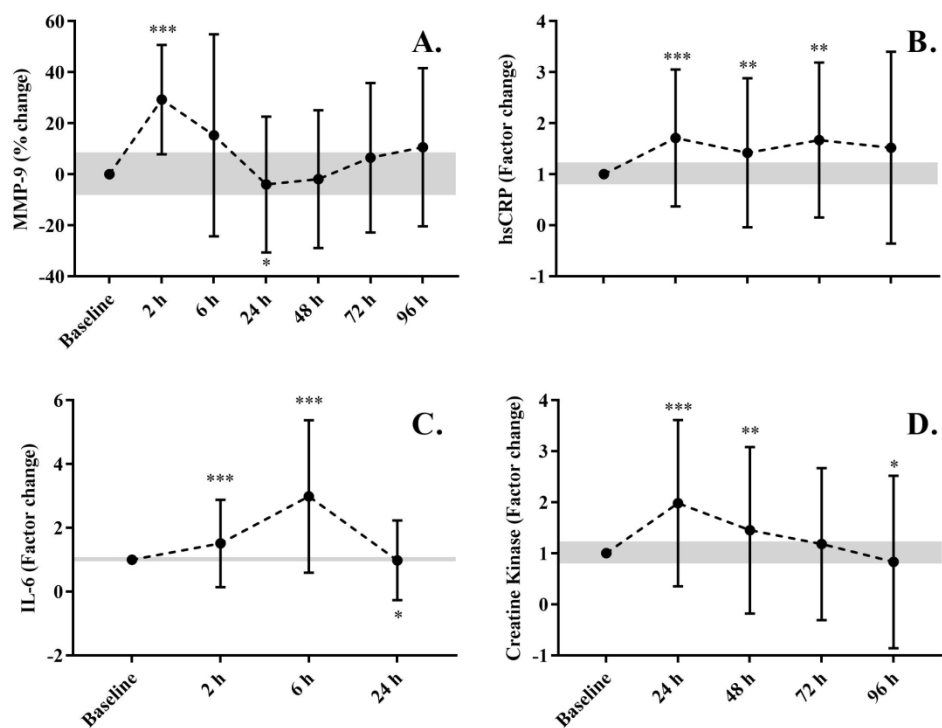


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