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Exercise-induced dehydration alters pulmonary function but does not modify airway responsiveness to dry air in athletes with mild asthma

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Running Head

Dehydration, pulmonary function and airway responsiveness.

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ABSTRACT

Background: Local airway water loss is the main physiological trigger for exercise-induced bronchoconstriction (EIB). **Aim:** To investigate the effects of whole-body water loss on airway responsiveness and pulmonary function in athletes with mild asthma and/or EIB. **Methods:** Ten recreational athletes with a doctor diagnosis of mild asthma and/or EIB completed a randomized, cross-over study. Pulmonary function tests (spirometry, whole-body plethysmography and diffusing capacity for carbon monoxide [DLCO]) were conducted before and after three conditions: i) 2 h exercise in the heat with no fluid intake (dehydration); ii) 2 h exercise with *ad libitum* fluid intake (control); and iii) time-matched rest period (rest). Airway responsiveness was assessed 2 h post-exercise/rest *via* eucapnic voluntary hyperpnea (EVH) to dry air. **Results:** Exercise in the heat with no fluid intake induced a state of mild dehydration, with a mean body mass loss of 2.3±0.8% (SD). After EVH, airway narrowing was not different between conditions: median (interquartile range) maximum fall in forced expiratory volume in 1 sec was 13 (7–15)%, 11 (9–24)% and 12 (7–20)% in the dehydration, control and rest conditions, respectively. Dehydration caused a significant reduction in forced vital capacity (300±190 ml, P=0.001) and concomitant increases in residual volume (260±180 ml, P=0.001) and functional residual capacity (260±250 ml, P=0.011), with no change in DLCO. **Conclusion:** Mild exercise-induced dehydration does not exaggerate airway responsiveness to dry air in athletes with mild asthma/EIB, but may affect small airway function.

NEW & NOTEWORTHY

This study is the first to investigate the effect of whole-body dehydration on airway responsiveness. Our data suggest that the airway response to dry air hyperpnea of athletes with mild asthma and/or exercise-induced bronchoconstriction is not exacerbated in a state of mild dehydration. Based on recorded alterations in lung volumes, however, exercise-induced dehydration appears to compromise small airways function.

KEY WORDS

Airway hyper-responsiveness, eucapnic voluntary hyperpnea, exercise-induced bronchoconstriction, exercise-induced asthma, whole-body dehydration.

INTRODUCTION

Whole-body dehydration commonly occurs in athletes engaging in endurance events (32), with loss of body mass frequently averaging 2-3% (31, 37). Whole-body dehydration is thought to limit exercise performance due to strain on multiple organ systems, including the circulatory, (central) nervous, muscular, integumentary, and urinary systems (8, 33). Lung fluid balance and water transport at pulmonary surfaces play an important physiological role in the maintenance of airway hydration and in proper airway clearance (16). Relatively little is known about the impact of whole-body dehydration on the respiratory system.

Only two studies have specifically investigated the effect of whole-body dehydration on pulmonary function (13, 15). A reduction in forced expiratory volume in one second (FEV_1) was noted in mildly dehydrated individuals following fluid deprivation (13). However, after diuretic (chlortalidone) drug administration, resulting in moderate dehydration, an increase in expiratory flow rates (including FEV_1) was subsequently noted (15). Therefore, uncertainty remains as to the impact of whole-body dehydration on the healthy human lung.

Equally uncertain is whether whole-body dehydration constitutes a significant risk factor for broncho-pulmonary disorders (16). A large body of evidence points toward acute dehydration of the airway surface liquid as a key determinant of exercise-induced bronchoconstriction (EIB) (2). EIB is characterized by a transient narrowing of the airways (with associated reduction in expiratory airflow) in response to vigorous exercise. Individuals most at risk for EIB are endurance athletes and patients with asthma (11, 17). During exercise-hyperpnea, water and heat are lost from the airway surface in response to humidifying large volumes of inspired (unconditioned) air over a short period of time (10).

87 The evaporative water loss is proposed to increase the osmolarity of the airway surface
88 liquid, particularly at the level of the small airways (9). This would then stimulate the
89 release of broncho-active mediators and cause, in susceptible individuals, the airway
90 smooth muscle to contract (2).
91
92 The primary provider of fluid to the airways is the bronchial circulation. Since exercise-
93 induced dehydration causes hypovolemia and increases blood plasma osmolarity (8),
94 alterations in the volume and composition of bronchial blood flow are to be expected in a
95 state of dehydration. Whole-body dehydration may therefore diminish airway surface
96 hydration, resulting in an amplified bronchoconstrictive response to exercise in individuals
97 with EIB.
98
99 The primary aim of this study was to establish the impact of whole-body dehydration,
100 induced by prolonged exercise in the heat, on airway responsiveness in athletes with a
101 prior medical diagnosis of mild asthma and/or EIB. Our hypothesis was that the fall in
102 FEV_1 after dry air hyperpnea would be exacerbated in a state of mild dehydration. Since
103 the effect of whole-body dehydration on resting pulmonary function remains uncertain, we
104 also assessed pulmonary function, *via* spirometry, whole-body plethysmography and
105 diffusing capacity for carbon monoxide, before and after induced dehydration.

METHODS

Participants

Ten recreational athletes (four female) completed the study. Mean age, height and body mass were: 21 ± 2 yr, 170 ± 12 cm and 63 ± 10 kg, respectively. Participants were involved in summer sports and trained for 6 ± 4 h *per* week in aerobic activities. All participants had a prior doctor diagnosis of mild asthma and/or EIB and reported respiratory symptoms (chest tightness, wheeze, mucus hyper-secretion, cough) during and/or after exercise. Five participants had childhood asthma, and eight were using short acting β_2-agonist medication. Participants taking any asthma medication other than inhaled short acting β_2-agonists or anti-histamines were excluded. Those on medication(s) were required to withhold inhaled short-acting β_2-agonists for a minimum of 8 h and anti-histamines for 72 h prior to each visit (4). All participants had baseline FEV_1 and FVC above the lower limit of normal (30). Participants were non-smokers, free from respiratory infection for 4 wk prior to the study, and had no known chronic medical condition other than asthma or EIB. All participants provided written informed consent. The institutional research ethics committee approved the study (ref#RE52-12).

Protocol

The study used a randomized crossover design with three experimental visits. The order of the experimental visits was randomized using the random number generator function in Microsoft Excel (2011), and visits were separated by >48 h. Pulmonary function was assessed using spirometry, whole-body plethysmography and diffusing capacity before and up to 2 h after each of the following conditions: i) exercise in the heat with no fluid intake (dehydration); ii) exercise with *ad libitum* fluid intake (control); iii) time-matched rest period (rest). To avoid influence of airway refractoriness (21), exercise intensity was set

low (cf. details below) and airway responsiveness was assessed 2 h after exercise. The 'rest' condition was included to further ensure that a refractory response was not present at the time of the bronchial challenge with dry air. To determine whether any changes caused by dehydration could be quickly reversed, a rehydration phase was included in the dehydration condition. In that condition, participants were allowed to drink water *ad libitum* between 20 and 60 min after the EVH challenge, after which final spirometry testing was performed. A schematic of the experimental protocol is presented in Figure 1.

All visits commenced in the morning so as to standardize for diurnal variation in pulmonary function (34). Participants were asked to withhold alcohol, caffeine and exercise on the day of testing.

Hydration status

Participants were asked to arrive at each experimental visit in a euhydrated state. Upon arrival, urine osmolality was measured using a portable refractive index osmometer (Osmocheck, Vitech Scientific Ltd, UK). Adequate hydration was defined as <700 $mOsmol \cdot kgH_2O^{-1}$ (32). Nude body mass was recorded before and 60 min after exercise or time-matched rest using a calibrated scale (SECA model 798, Hamburg, Germany), with the change in body mass used as the index of dehydration.

Exercise

In the control and dehydration conditions, participants completed 2 h of low intensity exercise. The exercise involved four bouts of 20 min of cycling, with each bout followed by 10 min of stepping. Cycling was performed at 25% of estimated peak power (14). Stepping was conducted on a 20 cm step at a rate of 45 steps *per* minute. Mid-way through each bout of exercise, heart rate was measured using telemetry (Polar H7, Polar

Electro (UK) Ltd, Warwick, UK) and minute ventilation using offline gas analysis (Douglas bags and Harvard dry gas meter). To induce dehydration, exercise was performed in an environmental chamber (Procema Ltd, Twickenham, UK) set at 37°C and 50% relative humidity and fluid intake was prohibited. In the control condition, environmental temperature was set at 20°C (ambient humidity) and fluid consumption was *ad libitum*. In the rest condition, participants remained seated in ambient conditions and were allowed to consume fluid *ad libitum*.

Pulmonary function

Pulmonary function was assessed using a commercially available system (Masterscreen, CareFusion, Hochberg, Germany). Spirometry was conducted at baseline and at 10 min and 120 min after exercise (or rest). Forced expiratory maneuvers were performed in accordance with ATS/ERS guidelines (25). Measurements were performed in triplicate, and the largest FEV_1 and FVC from reproducible maneuvers (i.e., between-maneuver differences <150 ml for FEV_1 and FVC) were kept for analysis. Following the EVH challenge, expiratory maneuvers were performed in duplicate (1). The GLI-2012 equations (30) were used for calculation of predicted values and lower limits of normal.

Whole-body plethysmography was used to determine static lung volumes and capacities according to ATS/ERS guidelines (35). Measurements were performed at baseline and at 60 min after exercise (or rest). The mean of three reproducible trials (i.e., the three functional residual capacity [FRC] values agreeing within 5%) was used for analysis. Residual volume (RV) was derived from the mean FRC minus mean expiratory reserve volume (ERV), and TLC was calculated as the sum of maximum vital capacity (VC) and RV.

Diffusing capacity of the lung for carbon monoxide (DLCO) was assessed using the single-breath technique according to ATS/ERS guidelines (23). The measurements were performed at baseline and at 90 min after exercise (or rest). The maneuver was repeated at least twice to ensure repeatability (i.e., <10% variation in DLCO). The mean DLCO, transfer coefficient (KCO), and alveolar volume (VA) were calculated from two reproducible maneuvers and used for analysis. Diffusing capacity data for one participant was lost due to technical error.

Airway responsiveness

Airway responsiveness to dry air was assessed *via* eucapnic voluntary hyperpnea (EVH) (1). Briefly, participants were asked to breathe for 6 min at a target ventilation of 85% predicted maximum voluntary ventilation (MVV, estimated as 30 × baseline FEV_1). A dry gas mixture of 21% O_2, 5% CO_2, and N_2 balance was delivered by a commercially available system (Eucapsys, SMTEC, Nyon, Switzerland). Ventilation was measured throughout the test, with participants receiving real-time visual feedback. The ventilation achieved during the first visit was set as the target ventilation for subsequent visits. Before and at regular time points after EVH (2, 5, 10, 15, 20 and 60 min), forced expiratory maneuvers were performed, with the maximum percentage change in FEV_1 from 'baseline' (i.e., the value recorded immediately pre-EVH) used as the index for airway responsiveness. A sustained ≥10% fall in FEV_1 (over two consecutive time-points) was consistent with a diagnosis of EIB (4).

Statistics

Sample size was based on previous studies that have investigated the effect of dehydration on pulmonary function (15) and EVH on airway caliber in recreationally active individuals (7, 18). Data were analyzed using statistical software (SPSS 20, Chicago, IL, US). Statistical significance was set at $P<0.05$ unless otherwise stated. Data were tested

for normality using the Shapiro-Wilk test. Data for the maximum fall in FEV_1 post-EVH were not normally distributed; therefore, differences between conditions were tested using a Friedman 2-way ANOVA by ranks test and data displayed as median and interquartile range (Q1-Q3). Resting spirometry, whole-body plethysmography and diffusing capacity data were normally distributed. Differences in resting pulmonary function between conditions and across times were analyzed using repeated-measures ANOVA with Bonferroni post-hoc analysis, as needed, and data are presented as mean ± SD. Heart rate and ventilation were averaged over the entire period of exercise and compared between dehydration and control conditions using paired t-test. Relationships between absolute changes in body mass and pulmonary function in the dehydration condition were assessed using Pearson's correlation coefficient.

RESULTS

Hydration status

Baseline body mass was not different across conditions (P=0.74). The dehydration intervention caused a significant reduction in body mass (63.3 ± 10.4 kg at baseline vs. 61.8 ± 10.1 kg post-exercise, P<0.001), which equated to a loss of 2.3 ± 0.8%. There was no change in body mass following exercise in the control condition (63.3 ± 10.5 kg at baseline vs. 63.1 ± 10.5 kg post-exercise, P=0.085) or over the rest period (63.2 ± 10.8 kg at baseline vs. 63.0 ± 10.7 kg post-rest, P=0.12). Over the rehydration period in the dehydration condition, participants drank 830 ± 190 ml of water (61 ± 19% of the loss in body mass).

Exercise

As expected, heart rate was significantly higher during exercise in the dehydration condition compared to the control condition (148 ± 16 vs. 118 ± 20 bpm, respectively; P<0.001). Ventilation did not differ significantly between conditions (42 ± 15 $l \cdot min^{-1}$ in the dehydration condition *vs.* 34 ± 6 $l \cdot min^{-1}$ in the control condition; P=0.084).

Airway responsiveness

Participants achieved a mean ventilation of 104 ± 29 $l \cdot min^{-1}$ during the EVH challenge over the three experimental visits, which corresponded to 70 ± 9% of predicted MVV. No difference in ventilation was noted across conditions (P=0.64). Seven participants (70%) had an EVH response consistent with a diagnosis of EIB in at least one condition. One additional participant had a transient fall in FEV_1 during one visit. The median and interquartile range for maximum reduction in FEV_1 post-EVH was 13% (7 – 15%), 11% (9 -

24%) and 12% (7 - 20%) in the dehydration, control and rest condition, respectively (Figure 2). These values were not different between conditions (P=0.20).

Dynamic lung function

At the start of the experimental visits, pulmonary function was not different between conditions (Table 1). However, an interaction effect was noted over time between conditions (P<0.001), with significant reductions in FVC only in the dehydration and control conditions (P<0.001 and P=0.014, respectively). In the dehydration condition, there was a sustained fall in FVC from baseline to 10 min (P=0.001) and 120 min of recovery (P=0.024), while in the control condition the reduction in FVC was only transient (i.e., noted only at 10 min of recovery) (Table 1). Further, the magnitude of change in FVC was greater under dehydration compared to both the control and rest conditions (Figure 3). In a state of dehydration, eight participants (80%) presented a clinically meaningful reduction in FVC (>200 ml), whereas only one participant demonstrated a >200 ml fall in FVC in the control condition and none in the resting condition. Following rehydration, FVC remained slightly, but significantly, lower than baseline (–90 ± 100 ml, P=0.022). No significant differences were noted between times and/or conditions for FEV_1 and PEF (Table 1).

Static lung function

Static lung volumes and capacities at baseline were not different between conditions (Table 2). Significant interaction effects were noted over the experimental conditions for FRC (P=0.004) and RV (P=0.001). In the dehydration condition, a significant increase in FRC was noted pre- to post-exercise (260 ± 250 ml, P=0.011); no difference was observed in the control or resting conditions (Table 2). A concurrent increase in RV of 260 ± 182 ml was observed under the dehydration condition (P=0.001) (Table 2). The magnitude of

change in FRC and RV from pre- to post-exercise was greater under dehydration compared to control (P=0.015 and P=0.060, respectively). Further, the change in RV was greater under dehydration compared to rest (P=0.005) (Figure 4). No significant changes were noted between times and/or conditions for ERV or TLC (Table 3). Consequently, RV/TLC was increased under dehydration (P<0.001) (Table 3).

Diffusing capacity

There were no differences in baseline DLCO, KCO or VA between conditions. Further, these variables were not modified by any of the conditions (Table 3).

Correlation analysis

There was a significant correlation (r^2=0.494, P=0.023) between the change in body mass and the change in RV at 60 min post-exercise in the dehydration condition (Figure 5). No other significant relationships were noted between study variables.

DISCUSSION

The aim of this study was to investigate the effects of exercise-induced dehydration on airway responsiveness and pulmonary function in athletes with a medical diagnosis of mild asthma and/or EIB. We showed that mild dehydration does not increase airway responsiveness to dry air hyperpnea, but is associated with alterations in lung volumes (i.e., reduced FVC and increased FRC and RV). Mild whole-body dehydration is therefore unlikely to put athletes at increased risk for EIB. However, perturbations at the level of the small airways are likely to occur when athletes with pre-existing lung condition become dehydrated.

This study is the first to assess the effect of whole-body dehydration on airway responsiveness. Given that athletes regularly experience exercise-induced dehydration (37) and that EIB is the most common chronic condition in elite athletes (11), these findings are highly relevant. We reasoned that whole-body dehydration may have the potential to affect the volume and/or composition of airway surface liquid and, consequently, could enhance the osmotic stimulus responsible for EIB (2). However, considering that no difference in the severity of bronchoconstriction was noted following EVH between the dehydration and control conditions, our data do not support this hypothesis.

To maintain ecological validity, we aimed to induce a state of mild dehydration using exercise. We were successful in that the average body mass loss was 2.3%. However, this mild degree of dehydration may have been insufficient to interfere with the pathophysiology of EIB. The volume of airway surface liquid is very small, with <0.5 ml of liquid covering the first seven generations of airways (5). Relative to the small volume of water available at the airway surface, airway water loss during hyperpnea of dry air is very

315 high. Based on mathematical modeling, the net water loss within the airways during
316 ventilation at 60 l·min^{-1} in temperate conditions and can exceed 0.4 ml·min^{-1} (10). It is
317 therefore possible that the large volume of respiratory water loss during EVH negated any
318 changes in airway surface liquid induced by our dehydration protocol.
319
320 An alternative explanation for why airway responsiveness was unaffected by whole-body
321 dehydration is that EVH provoked a maximal airway response. A maximum response
322 plateau has been shown to occur following bronchial provocation with exercise in children
323 with asthma, with no further increase in the severity of EIB beyond six minutes of exercise
324 (12). This raises the possibility that the use of EVH as bronchial stimulus may have
325 masked the effects of whole-body dehydration on airway responsiveness. To address this
326 issue, future work should be conducted using a dose-response bronchial challenge, such
327 as the mannitol test (22). Further, since a maximal response plateau occurs less frequently
328 in individuals with a greater degree of airway responsiveness (36), our findings should not
329 be generalized to individuals with moderate-to-severe asthma/EIB.
330
331 A concurrent aim of our study was to investigate the effect of exercise-induced dehydration
332 on basal pulmonary function. In contrast to previous research (13, 15), our results suggest
333 that dehydration causes a reduction in FVC (with no associated change in FEV_1).
334 Previously, induced dehydration, by either fluid deprivation (13) or diuretic drug
335 administration (15), had no effect on FVC. However, both interventions caused either a
336 decrease (11) or an increase (13) in FEV_1, with the latter finding attributed to a decrease in
337 airway resistance secondary to a reduction in water content in the airway mucosa and
338 bronchovascular sheath or a decrease in pulmonary vascular volume (13). The
339 discrepancy in results may be due to the various protocols employed. Fluid deprivation for
340 16 h resulted in smaller decreases in body mass than noted in the current study (range:

0.0 to 2.5% (13) *vs.* 1.5 to 4.4% in our study). While a more pronounced state of dehydration was induced by diuretics (~4.5 % loss of body mass) (15), the different types of water loss (hypertonic *vs.* isosmotic) may have influenced the results. Exercise-induced dehydration is well known to increase plasma osmolarity, whereas dehydration induced *via* diuretic administration generally results in isosmotic hypovolemia (33). In the present study, the increase in plasma osmolarity might have caused a redistribution of fluid away from the airways, which, in turn, may have affected lung volumes. That an inverse relationship was found in a large (>10,000) adult population between serum osmolarity and FVC (29) supports the idea that hypertonic dehydration may adversely affect pulmonary function.

In our study, the reduction in FVC was associated with a concomitant increase in RV, FRC and RV/TLC ratio; the latter a marker of air trapping (19). Further, a positive association was found between the degree of dehydration (as inferred by the reduction in body mass) and the increase in RV. Together, these results suggest that exercise-induced dehydration primarily affects the small airways. We propose that the main underlying mechanism for these changes is reduced peripheral airway stability caused by a change in the properties and/or volume of airway surface liquid in a dehydrated state. Airway surface liquid has low surface tension, which inhibits small airway closure at low lung volumes (24). If exercise-induced dehydration increases airway surface tension, it would explain the reduction in FVC and the increase in RV.

Our data show that mild exercise-induced dehydration results in sustained, clinically significant reductions in FVC [>200 ml (28)] in the majority of athletes with mild asthma/EIB. Due to controversy over a potential impairment of airway secretions in individuals with asthma (20, 26, 27), our findings may not be applicable to all athletes.

Nonetheless, considering the widespread prevalence of asthma/EIB in elite athletes (11), the functional relevance of these findings deserves further attention. That end-expiratory lung volume decreases with exercise and that dehydration may affect peripheral airway stability at low lung volumes, it is tempting to speculate that exercise-induced dehydration may increase the risk of cyclic opening and closure of peripheral airways during exercise. *In vitro*, the re-opening of closed airways can cause epithelial injury (6). As repeated epithelial injury is regarded as a key mechanism in the pathogenesis of EIB in athletes (3), these findings could be highly relevant in the context of EIB.

In conclusion, whole-body dehydration does not exacerbate airway responsiveness to dry air hyperpnoea in recreational athletes with mild asthma/EIB. However, lung volumes (incl. FVC, RV, FRC and RV/TLC) could be compromised in a state of mild dehydration. The functional and clinical relevance of these novel findings are yet to be established.

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Disclosure

None

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Figure Captions

Figure 1. Schematic of protocol to assess changes in airway responsiveness and pulmonary function in a dehydration condition (2 h of exercise in the heat with fluid restriction), a control condition (2 h of exercise in ambient conditions with voluntary fluid consumption), and a time-matched rest condition (2 h of rest with voluntary fluid consumption). EVH, eucapnic voluntary hyperpnea; DLCO, diffusing capacity of the lung for carbon monoxide; $\dot{V}_E$, ventilation; HR, heart rate.

Figure 2. Change in forced expiratory volume in 1 sec (FEV_1) after: i) exercise in a dehydrated state (dehydration), ii) exercise in a euhydrated state (control), and iii) a time-matched rest condition (rest). Data are for ten recreational athletes with mild asthma and/or exercise-induced bronchoconstriction. Data are median and inter-quartile range.

Figure 3. Change in forced vital capacity (FVC) after: i) exercise in a dehydrated state (dehydration), ii) exercise in a euhydrated state (control), and iii) a time-matched rest condition (rest). Data are for ten recreational athletes with mild asthma and/or exercise-induced bronchoconstriction. Data are mean ± 95% confidence interval. * P≤0.05, different vs. control and rest; ** P≤0.01 different vs. control and rest. Reduction in FVC >200 ml (---) is considered clinically meaningful (28).

Figure 4. Change in functional residual capacity (FRC) and residual volume (RV) after: i) exercise in a dehydrated state (dehydration), ii) exercise in a euhydrated state (control), and iii) a time-matched resting condition (rest). Data are for ten recreational athletes with mild asthma and/or exercise-induced bronchoconstriction. Data are mean ± 95% confidence interval.

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530 **Figure 5.** Relationship between change in body mass and change in residual volume (RV)

531 after 2 h of exercise with fluid restriction.

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538 **Table 1.** Dynamic lung indices at baseline and after: i) exercise in a dehydrated state
539 (dehydration), ii) exercise in a euhydrated state (control), and iii) a time-matched rest
540 period (rest).

		Dehydration	Control	Rest
FEV_1 (l)	Baseline	4.21 ± 0.89	4.17 ± 0.87	4.18 ± 0.85
	10 min post	4.24 ± 0.90	4.21 ± 0.96	4.28 ± 0.90
	120 min post	4.23 ± 0.89	4.24 ± 0.93	4.31 ± 0.92
	Rehydrated (60 min post-EVH)	4.19 ± 0.94	4.10 ± 0.90	4.10 ± 0.81
FVC (l)	Baseline	5.09 ± 1.22	5.09 ± 1.23	5.12 ± 1.19
	10 min post	4.79 ± 1.10*^{CR}	5.00 ± 1.21*^{R}	5.10 ± 1.17
	120 min post	4.89 ± 1.10*^{CR}	5.06 ± 1.20	5.17 ± 1.25
	Rehydrated (60 min post-EVH)	5.00 ± 1.20*	5.03 ± 1.25	5.06 ± 1.21
PEF ($l \cdot s^{-1}$)	Baseline	9.13 ± 2.25	9.13 ± 2.13	9.20 ± 2.10
	10 min post	9.16 ± 2.01	9.47 ± 2.47	9.64 ± 2.44
	120 min post	9.12 ± 2.16	9.36 ± 2.31	9.62 ± 2.32
	Rehydrated (60 min post-EVH)	8.90 ± 2.17	9.10 ± 2.40	8.89 ± 1.94

541
542 Data are mean ± SD for 10 participants. FEV_1, forced expiratory volume in 1 s; FVC,
543 forced vital capacity; PEF, peak expiratory flow. * $P<0.05$, different versus baseline; ^{C}
544 $P<0.05$, different versus control at corresponding time point; ^{R} $P<0.05$, different versus rest
545 at corresponding time point.
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549 **Table 2**. Static lung volumes and capacities at baseline and after: i) exercise in a
550 dehydrated state (dehydration), ii) exercise in a euhydrated state (control), and iii) a time-
551 matched rest period (rest).
552

		Dehydration	Control	Rest
TLC (l)	Baseline	6.70 ± 1.58	6.72 ± 1.55	6.72 ± 1.66
	60 min post	6.74 ± 1.61	6.66 ± 1.62	6.71 ± 1.59
FRC (l)	Baseline	3.40 ± 0.99	3.46 ± 1.02	3.49 ± 0.97
	60 min post	3.65 ± 0.90*^{C}	3.35 ± 0.95^{R}	3.55 ± 1.02
RV (l)	Baseline	1.73 ± 0.46	1.76 ± 0.45	1.77 ± 0.55
	60 min post	1.99 ± 0.57*^{C}	1.74 ± 0.51	1.81 ± 0.59
ERV (l)	Baseline	1.67 ± 0.64	1.71 ± 0.67	1.72 ± 0.61
	60 min post	1.67 ± 0.48	1.61 ± 0.56	1.74 ± 0.66
RV/TLC (%)	Baseline	25.9 ± 2.9	26.1 ± 2.5	26.2 ± 3.1
	60 min post	29.3 ± 2.9*^{C}	26.1 ± 3.0	26.8 ± 4.5

553
554 Data are mean ± SD for 10 participants. TLC, total lung capacity; FRC, functional residual
555 capacity; RV, residual volume; ERV, expiratory reserve volume; * P<0.05, different versus
556 baseline; ^{C} P<0.05, different versus control at corresponding time point; ^{R} P<0.05, different
557 versus rest at corresponding time point.
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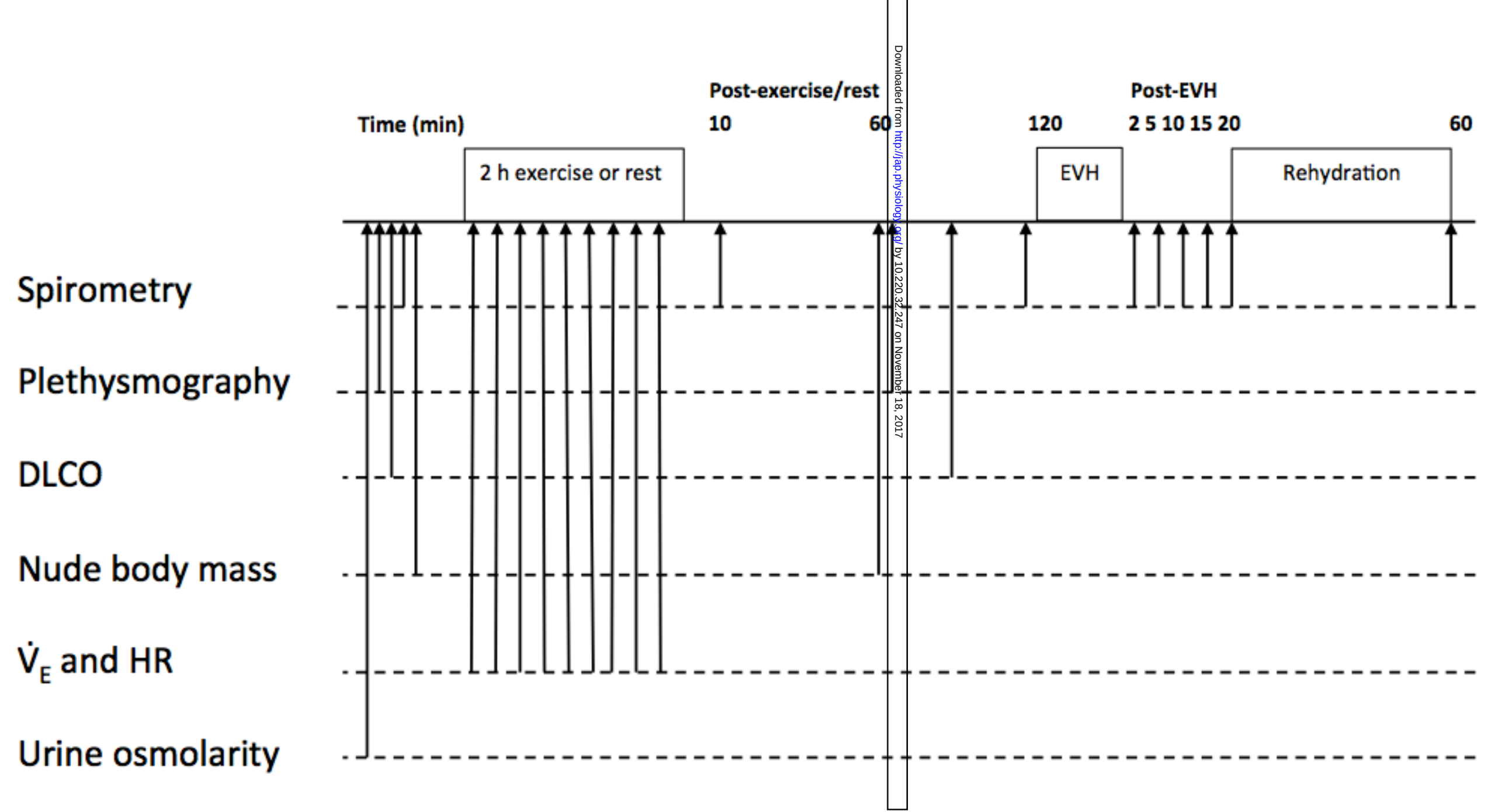
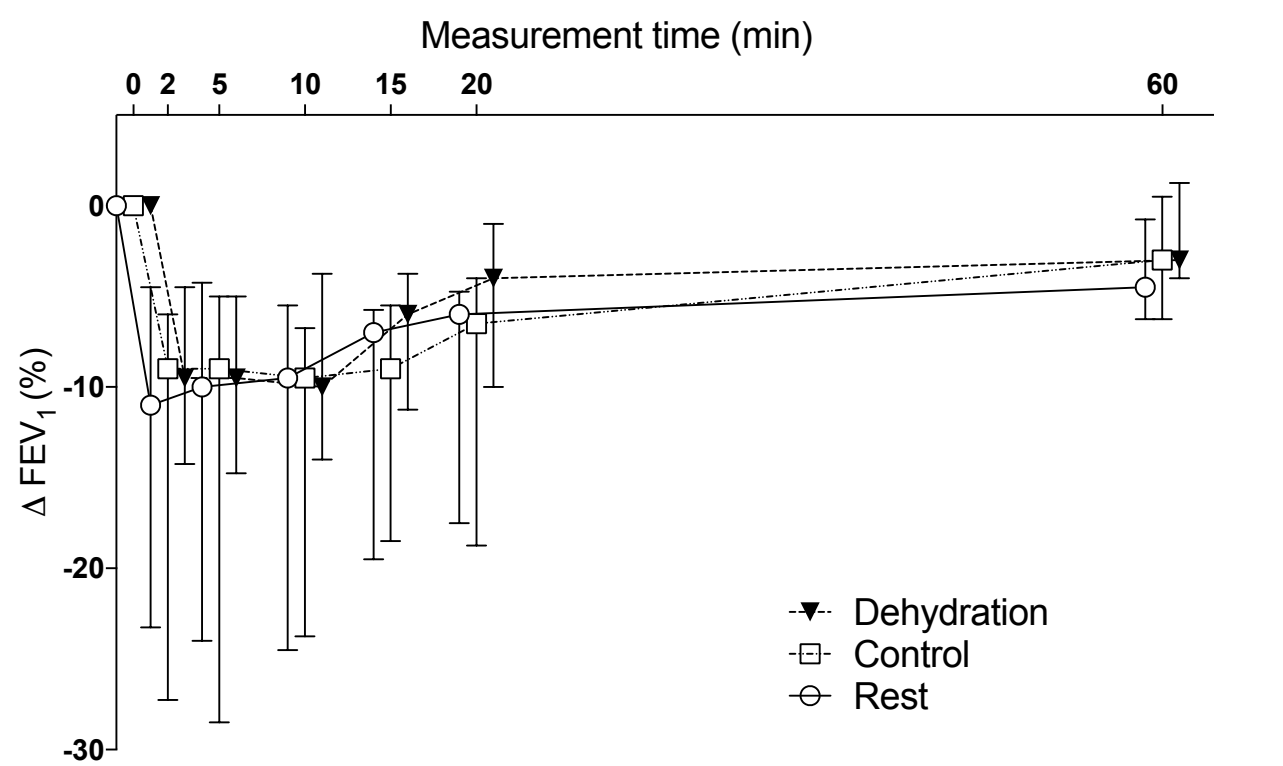
564 **Table 3**. Indices of diffusing capacity at baseline and after: i) exercise in a dehydrated
565 state (dehydration), ii) exercise in a euhydrated state (control) and iii) a time-matched rest
566 period (rest).
567

		Dehydration	Control	Rest
DLCO ($mmol \cdot min^{-1} \cdot kPa^{-1}$)	Baseline	10.14 ± 2.81	9.92 ±2.69	10.16 ± 2.87
	90 min post	10.07 ± 2.85	9.72 ± 2.53	9.71 ± 2.61
KCO ($mmol \cdot min^{-1} \cdot kPa^{-1} \cdot l^{-1}$)	Baseline	1.65 ± 0.22	1.65 ± 0.25	1.63 ± 0.27
	90 min post	1.63 ± 0.20	1.60 ± 0.22	1.57 ± 0.25
VA (l)	Baseline	6.16 ± 1.55	6.05 ± 1.45	6.13 ± 1.51
	90 min post	6.18 ± 1.58	6.13 ± 1.50	6.21 ± 1.53

568 Data are mean ± SD for 9 participants. DLCO, diffusing capacity of the lung for carbon
569 monoxide; KCO transfer coefficient, VA alveolar volume.

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5
10
15
20
60
0
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-20
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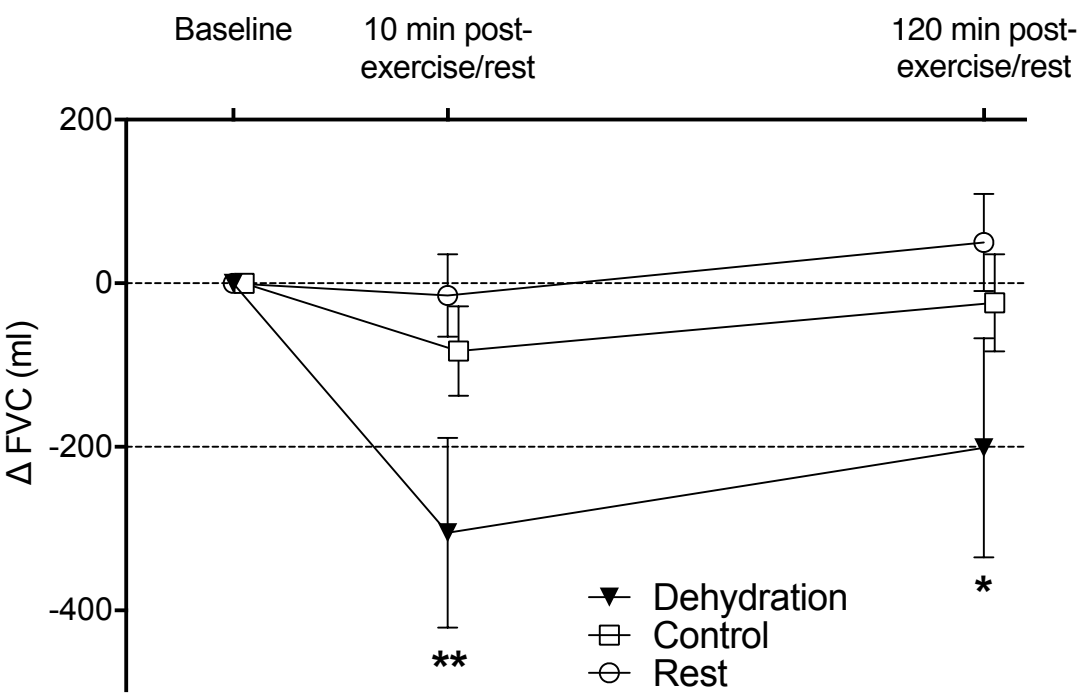
Δ FEV1 (%)
Dehydration
Control
Rest


Baseline
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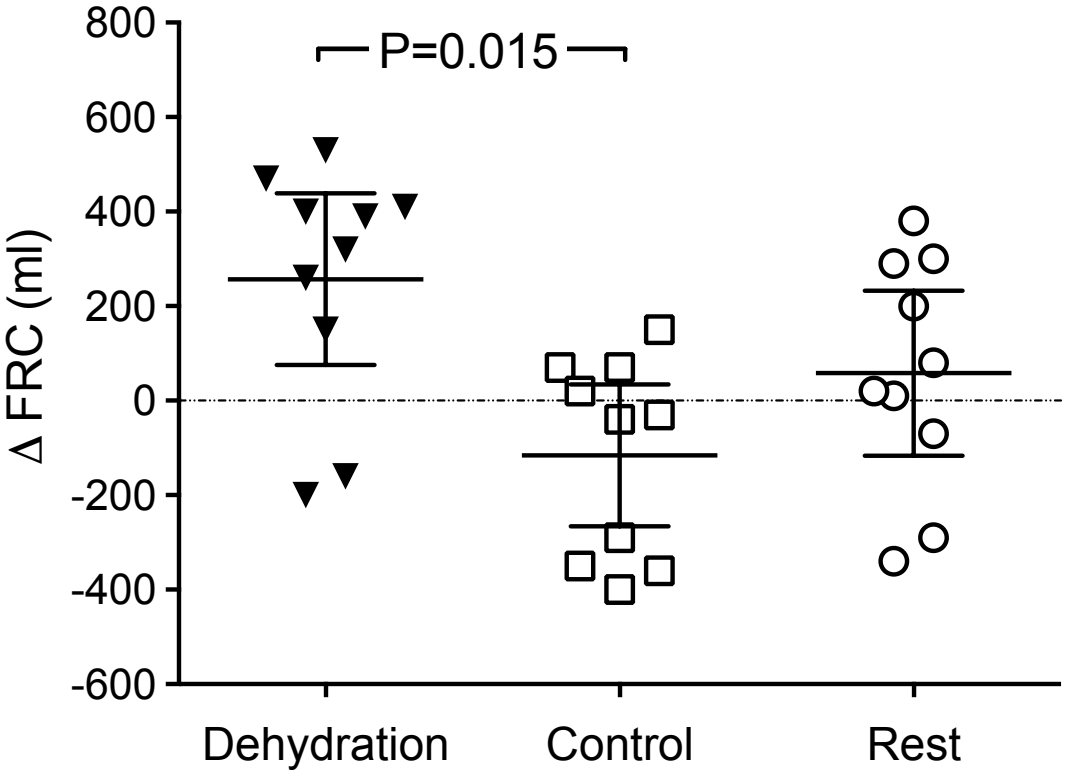
120 min post-exercise/rest
200
0
-200
-400
Δ FVC (ml)
**
*
Dehydration
Control
Rest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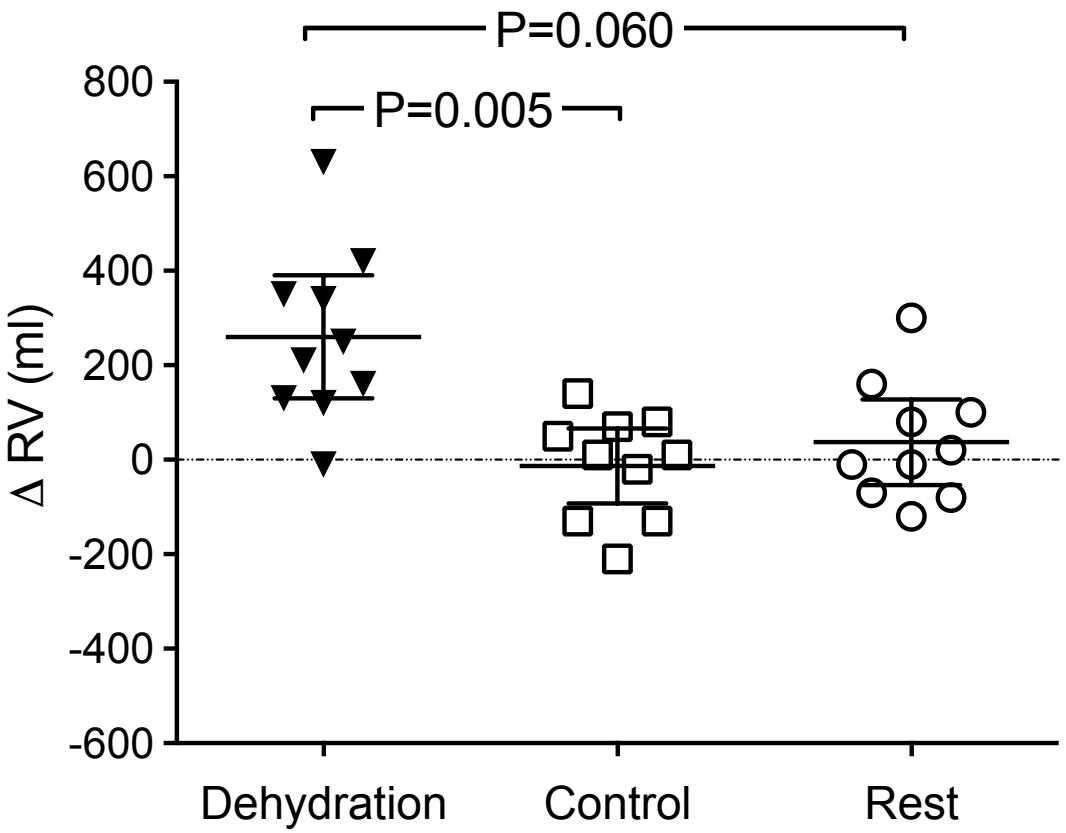
Δ FRC (ml)
Dehydration
Control
Rest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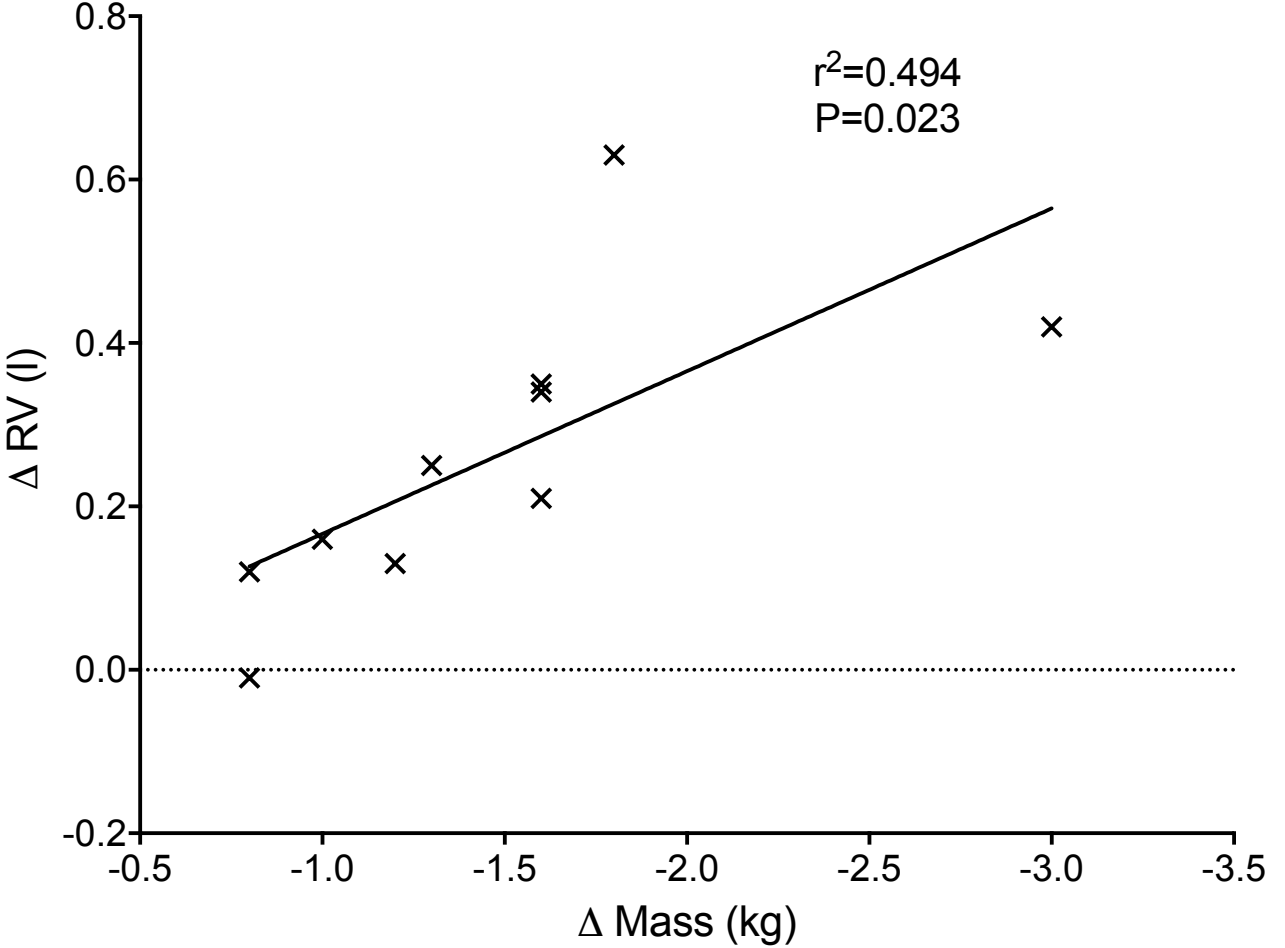
Δ RV (ml)
Dehydration
Control
Rest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0.4
0.2
0.0
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Δ RV (l)
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-1.0
-1.5
-2.0
-2.5
-3.0
-3.5
Δ Mass (kg)