Thirst-guided participant-controlled intravenous fluid rehydration: a single blind, randomised crossover study

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Abstract

Background: Dehydration is prevalent in healthcare and is associated with increased mortality and morbidity. Clinical assessment and diagnostic measures of dehydration are unreliable. We sought to investigate the novel concept that individuals might control their own intravenous rehydration, guided by thirst.

Methods: We performed a single-blind, counterbalanced, randomised cross-over trial. Ten healthy male volunteers of mean age 26 (SD=10.5) years were dehydrated by 3-5% of their baseline body mass by exercising in the heat (35°C, 60% humidity). This was followed by a 4-hour participant-controlled intravenous rehydration: individuals triggered up to 6 fluid boluses (4% dextrose in 0.18% sodium chloride) per hour in response to thirst. Participants undertook two blinded rehydration protocols which differed only by bolus volume: 50mL (low volume, LV) or 200mL (high volume, HV). Each hour during the rehydration phase, plasma osmolality (pOsm) was measured and thirst score recorded. Nude body mass was measured at baseline, post-dehydration and following the rehydration phase.

Results: In both conditions, mean dehydration-related body mass loss was 3.9%. Thirst score was strongly associated with pOsm (within-subject r=0.74) and demand for fluid fell as pOsm corrected. In the HV condition, participants rapidly rehydrated themselves (mean fluid delivered 3060mL vs 981mL in the LV condition) to body mass and pOsm no different to euhydrated state.

Conclusion: Healthy individuals appear able to rely on thirst to manage intravenous fluid intake. Future work must now focus on whether *patient*-controlled intravenous fluids could represent a paradigm shift in the management of hydration in the clinical setting.

Key words: Body Water; Dehydration; Fluid Therapy; Osmolar Concentration; Thirst

Introduction

Water is critical for survival: it is the largest single component in the human body and is necessary for numerous essential physiological processes. Dehydration, a deficit in body water content, is prevalent in clinical environments[1–3] and associated with increased mortality and morbidity.[3–8] However, clinical dehydration is a continuum rather than a binary state and has no internationally-recognised definition. Associated clinical signs can be subtle and unreliable, and there is no objective marker with everyday clinical utility.[9–11] As a consequence, diagnosis of clinical dehydration is frequently delayed or missed, and prompt rehydration strategies are often poorly delivered in healthcare environments.[1] Thirst plays an integral part in body water homeostasis.[12,13] Plasma osmolality (pOsm) is considered the most reliable surrogate objective marker of dehydration[9] and will increase with uncompensated water loss. Increased osmolality is sensed by hypothalamic osmoreceptors stimulating thirst and pituitary secretion of antidiuretic hormone (ADH).[14] Thirst is sensitive to small changes in pOsm and shows little intra-individual variation.[15] Hypovolaemia, in addition to hyperosmolarity, also triggers thirst through angiotensin II and baroreceptor-mediated mechanisms.[16] It is thus rational to propose tendering control of intravenous rehydration to patients, enabling them to use the finely-honed intrinsic thirst mechanism (where this is considered intact) to guide their own fluid therapy. A recent pilot study showed that healthy male volunteers, dehydrated by oral furosemide (40 mg) and 12 h of oral fluid restriction, rehydrated themselves more efficiently intravenously when guided by thirst than when receiving a national guideline-based, clinician-delivered fluid regimen.[17] However, the study was unblinded, making it liable to subject bias. We thus designed the present study to address this issue. We hypothesized that: the demand for self-administered intravenous fluid in response to thirst would be related to the degree of dehydration; that the rate of self-administration would reduce in frequency in proportion to the degree of correction of fluid deficit; and that the rate of fluid administration would be impacted by the volume of the bolus of fluid administered on each administration.

Methods

Participants

Healthy, physically active adult (18 – 65 years) males were recruited from the staff and student populations at the authors' affiliated institutions. Potential participants identified themselves by responding to study advertisements (emails and posters). Excluded were those with cardiovascular, renal or hepatic disease; those with history of heat intolerance (where the dehydration protocol might carry risk); and those taking medications which might affect sense of thirst or salt/water handling. The final decision on study eligibility was dependent upon physician review of a detailed health questionnaire.

Participants attended the Extreme Environments Laboratory (EEL) at the University of Portsmouth on two occasions separated by at least seven days. They were randomly allocated (using software provided by *randomizer.org*) to a balanced cross-over design. The *pre-intervention phase* established the euhydrated state of participants and was indentical in each condition of the trial. The *intervention phase* involved the dehydration of participants by exercise in a warm humid environment, followed by participant-controlled intravenous rehydration. The intervention phase differed between conditions in the volume of self-administered fluid boluses (low or high volume boluses: 50 or 200 mL respectively). The phases are described in detail in the sections below.

Pre-Intervention phase

For the three days before attending the EEL, participants were provided with 30 $mL.kg^{-1}$ of isotonic fluid (*NectarHydro* electrolyte tablets, *For Goodness Shakes* Ltd, UK: 1 tablet per 750 mL of water) that was consumed between 08:00 and 24:00hrs, each day. Additional fluid was drunk *ad libitum*. Each morning, following an overnight fast, the participant recorded a nude, post-void body mass using scales provided by the investigating team (Salter 9206, *Salter Housewares*, UK). The average of the three body mass measurements was considered as the baseline euhydrated mass from which the

degree of dehydration (%) was determined.[18,19] For the duration of these three days, participants ate a normal diet but were instructed to refrain from strenuous exercise.

Intervention phase – dehydration protocol

Participants arrived at the EEL after an overnight fast and having refrained from alcohol, caffeine, tobacco and all forms of exercise for 12 hours. After providing a urine sample for urine osmolality, participants recorded their third and final nude/post-void body mass (using the same scales as for previous measurements). Having rested in the semi-recumbent position for 15 minutes (to account for postural effects on plasma volume) 6 mL of venous blood was drawn for pOsm measurement: the blood was collected into lithium heparin plasma collection tubes (*BD Vacutainer*, UK), centrifuged (4500 g for 10 minutes at 4°C) and pOsm measured (3320 Micro-Osmometer, *Advanced Instruments,* USA) in duplicate and the mean value used for data analysis. A triplicate value was used if the duplicate values differed by >5 $mOsm.kg^{-1}$, in which case the mean of the two closest values was used. Resting heart rate, non-invasive blood pressure and deep body (rectal) temperature were also recorded (details below). A standardised, high carbohydrate breakfast of known mass was provided (two slices of bread, jam and butter; ~150 g) after baseline measures.

Each participant was gradually dehydrated to a target range of 3-5 % reduction in body mass using exercise-heat stress in the climatic chamber of the EEL. This involved intermittent exercise on bicycle ergometers (Wattbike Trainer, *Wattbike Ltd,* UK) at 35 °C and 60 % relative humidity to elicit and maintain a target rectal temperature of 38.5°C. Participants were instructed to cycle at a hard work rate equivalent to a Rating of Perceived Exertion (RPE) of 15 using the 6-20 RPE scale[20] until the target rectal temperature was achieved, and reduce the work rate thereafter to maintain that temperature.[21] After each 30 minute period of exercise, there was a 10 minute rest during which body mass was measured. This 40 minute protocol was repeated until the dehydration process was complete: either a 3-5 % reduction in body weight had been achieved or 4 hours had elapsed. At the end of every 90

minutes the participant was given a standardised snack to eat (banana; ~50g). When the participant repeated the dehydration process for the other condition they used exactly the same methodology and dehydration target. Rectal temperature was measured continuously whilst in the chamber using a rectal thermistor inserted to a depth of 15 cm and recorded using a data logger (Squirrel 2040, *Grant Instruments Ltd*, UK). Heart rate was measured continuously using a *Polar*® monitor (RS800, *Polar Electro*, Finland). Non-invasive blood pressure measurements were taken every 30 minutes using an automated blood pressure machine (Omron M5-I, *Omron,* UK).

Intervention Phase – participant-controlled rehydration

On completion of the dehydration process, participants were towel dried, transferred from the chamber to a separate climate-controlled room (~21 °C) and a final nude post-void body mass recorded. After 15 minutes in the semi-recumbent position a venous cannula (*BD Venflon*, UK) was inserted in the dorsum of the hand, and a 6 mL venous blood sample was drawn for pOsm measurement. A contemporaneous thirst score was recorded using a 10 cm visual analogue scale (0cm "not thirsty" to 10cm "extremely thirsty"), after which the intravenous fluid regimen was started.[15] Intravenous fluid was delivered by volumetric pump (*Infusomat; B Braun Medical*, UK). In both the 'lower volume' (LV) fluid bolus condition and the 'higher volume' (HV) fluid bolus condition a continuous background infusion of 4 % dextrose in 0.18 % sodium chloride at 50 $mL.h^{-1}$ was delivered for the entire 4 hour rehydration period. Participants were given a handset with demand button which, when pressed, delivered an additional volume of fluid from the infusion pump; this was administered over a 10-minute period (thus allowing a maximum of 6 boluses per hour). In the LV condition, the trigger delivered 50 mL over 10 minutes at a rate of 300 $mL.h^{-1}$. In the HV condition, the trigger delivered 200 mL over 10 minutes at a rate of 1200 $mL.h^{-1}$. A green visual signal indicated to the participant that no additional infusion was running, and that pressing the demand button would activate delivery of another bolus. A red visual signal indicated to the participant that a bolus was running, and that pressing the demand button would have no effect. The time at which each bolus

was demanded by the participant was recorded by a member of the investigating team. Each participant completed both conditions with a minimum of 7 days separating each condition.

The participant was blinded to which bolus volume they were receiving. This was achieved using various means: fluid bags and pumps were hidden from view; over-ear headphones were worn with music played during the intervention phase, to mask any noise of the pump (albeit that this was considered undetectable); the duration of the on-demand fluid bolus was the same, regardless of whether the HV or LV condition was in process; the constant low-rate background fluid infusion helped make the participant less aware of bolus infusions, helping to blind them from the size of the bolus; to further disguise the infusion, a cool damp towel was placed over the arm at the site of infusion.[22] At the end of the first hour of the protocol a second cannula was inserted in the antecubital vein of the contralateral arm. Another 6 mL venous sample was drawn on insertion for pOsm. Further samples were drawn every hour during the rehydration phase: the first 4 mL volume drawn from the cannula was discarded, and the subsequent 6 mL used for analysis. Cannula patency was maintained with 1 mL flush of 0.9 % sodium chloride every 15 minutes and 2 mL flush after blood withdrawal (total of 5 mL each hour); blood withdrawal for pOsm was always at least 15 minutes after any flush. Thirst intensity was recorded at the same time as each blood sample draw. Non-invasive blood pressure and heart rate were measured every hour. After 4 hours the rehydration protocol was complete.

Statistical Analysis

We recruited 10 participants with a convenience sample approach. A power calculation indicted that a sample size of ten participants would be sufficient to detect a difference between conditions in plasma osmolality of 2.13 ± 1.3 $mOsm.kg^{-1}$ (reported coefficient of variation of the microosmometer) with an alpha level set at P=0.05 (two tailed) and 90% power. Statistical analyses were undertaken using SPSS Version 25 (*IBM*, USA) and Stata Version 14 (*StataCorp*, USA). Significance was set *a priori* at $P \leq 0.05$ and data are presented as mean (SD) unless otherwise stated. Data were checked for

normality using the Shapiro Wilk and Kolmogorov Smirnov tests. Differences between conditions were analysed by paired *t*-test. Where repeated measurements were made over multiple time points, data were analysed by two-way repeated measures ANOVA (condition × time). Sphericity was assessed using Mauchly's test, with the Greenhouse-Geisser statistic employed to account for violations of sphericity. Significant main and interaction effects were explored post-hoc using Student's *t*-test for paired data. Where a main effect for time was evident, *a priori* planned post-hoc comparisons were made relative to baseline data and/or end of dehydration phase data only. Count data (frequency of "push" of the demand button) was analysed using mixed effects Poisson regression. The coefficient of variation was calculated according to Hopkin's reliability spreadsheet (sportsci.org). Within- and between-subject correlations were calculated using the methods described by Bland and Altman.[23,24] Curve fitting was undertaken using the curve fitting function in MATLAB (*MathWorks* Inc., USA).

Study Approval

Written informed consent was obtained from all participants and the study complied with the standards set by the Declaration of Helsinki. Ethical approval was obtained from the University of Portsmouth Science Faculty Ethics Committee (reference SFEC 2018-053A) and trial registration was completed with clinicaltrials.gov (NCT03932890).

Results

Participants

Eleven men were screened for eligibility: all fulfilled inclusion criteria and were recruited to the study. One of the participants reported feeling unwell during the dehydration protocol in the EEL and subsequently withdrew from the study before completing both conditions. Only the data from the 10 participants that completed both study conditions were included in the analysis. The included participants had a mean(SD) age of 26(10.5) years and body mass 79(7.4) kg.

Pre-Intervention phase

Body mass was stable across the three morning measurements prior to the dehydration and rehydration intervention ($F_{2,18}$ = 0.320, P = 0.730), with no differences between conditions ($F_{1,9}$ = 0.363, P = 0.562) and no interaction effect ($F_{2,18}$ = 0.161, P = 0.853). The average coefficient of variation for body mass over the three morning measurements was 0.6 %, for both conditions of the study. Mean(SD) baseline pOsm was 291.2(3.2) and 292.0(2.0) $mOsm.kg^{-1}$ for the LV and HV conditions respectively, with a baseline Uosm of 653(190) and 645(165) $mOsm.kg^{-1}$ for LV and HV conditions, respectively. Neither measure differed between conditions (pOsm: t_9 = -0.91, P = 0.387; Uosm: t_9 = 0.14, P = 0.889) pre-intervention.

Intervention phase

Body mass over the course of the intervention phase of the study is shown in Figure 1a. A significant main effect of time indicated that body mass changed over the course of the intervention ($F_{2,18}$ = 197.265, P < 0.001), and although the main effect of condition ($F_{1,9}$ = 4.295, P = 0.068) was not significant, the interaction of condition × time was significant ($F_{2,18}$ = 131.302, P < 0.001). Post-hoc analysis of the time and interaction effects indicated that body mass was not different between-conditions at baseline and was decreased to a similar extent by the dehydration intervention. This was equivalent to a 3.9(0.8) % and 3.9(0.6) % body mass loss, for the LV and HV conditions, respectively.

Following the rehydration phase, body mass had increased in both conditions, but to a greater extent in the HV condition where the final body mass was not different from the baseline body mass (P = 0.907).

The thirst scores following the dehydration phase and over the course of the rehydration phase of the experiment are shown in Figure 1b. There was a significant main effect of time ($F_{1.8,16.3}$ = 67.989, P < 0.001) and condition ($F_{1,9}$ = 10.558, P = 0.010) on thirst, although the interaction effect was not significant ($F_{4,36}$ = 2.122, P = 0.098). Post-hoc analysis indicated that the dehydration intervention elicited a similar high thirst score in both conditions. Thereafter thirst score was significantly diminished in both conditions, with the thirst score being lower in the HV than LV condition until the end of the rehydration period.

“Push” frequency (number of times that the delivery button was pressed) data are shown in Figure 1c. There was a significant time effect by condition interaction (P = 0.019). In the first hour of the rehydration protocol, participants requested fluids at the near maximal frequency possible, in both groups. Thereafter, in the HV condition “push” frequency was reduced by the third hour (P = 0.008) and by the fourth hour the incident rate ratio (IRR) compared to baseline was 0.2 (95% CI: 0.11-0.38), P <0.0001. A significant reduction in push frequency did not occur until the fourth hour in the LV condition (IRR (95% CI) = 0.63 (0.42-0.95), P = 0.026). During the final hour of the rehydration phase the push frequency was significantly lower in the HV group than in the LV condition (IRR (95% CI) = 0.32 (0.17-0.62), P = 0.001). Over the course of the rehydration phase the total volume of fluid delivered to the participants was greater in the HV condition, mean(SD): HV 3060(501) mL; LV 981(167) mL (t_9 = -13.980, P <0.001).

POsm data at baseline, and following the dehydration and rehydration phases of the protocol, are shown in Figure 1d. There were significant main (time: $F_{5,45}$ = 35.349, P < 0.001; condition: $F_{1,9}$ = 37.918,

$P < 0.001$) and interaction effects ($F_{5,45} = 8.214$, $P < 0.001$). Following the dehydration phase, pOsm was elevated to a similar extent in both conditions. Thereafter, in the HV condition, pOsm was reduced from 1 hour of the rehydration protocol onwards, and after 3 hours of the rehydration protocol was not different from baseline ($P = 0.501$). In contrast, in the LV condition, pOsm was not reduced until 3 hours of the rehydration protocol, but remained above baseline values throughout the rehydration phase and was higher than in the HV condition from 2 hours onwards.

Figure 2a shows the mean pOsm following the dehydration phase and for each hour of the rehydration phase, plotted against the corresponding mean thirst score, for both conditions. An exponential equation shows that these data were strongly associated (between-subject $r = 0.99$, within-subject $r = 0.74$), indicating that pOsm was related to thirst in a similar way, irrespective of fluid delivery rate. Figure 2b shows mean pOsm following the dehydration phase and for each hour of the rehydration phase, plotted against the corresponding push frequency for both conditions. These data were well described by a linear equation (between-subject $r = 0.98$, within-subject $r = 0.66$). The zero push intercept of the median push frequency *vs*. mean pOsm regression was 289 $mOsm.kg^{-1}$, suggesting that the participants would stop requesting fluids at this pOsm level. Finally, Figure 2c shows mean thirst score following the dehydration phase and for each hour of the rehydration phase, plotted against the corresponding push frequency for both trials, these data were well described by an inverse exponential relationship (between-subject $r = 0.99$, within-subject $r = 0.87$).

Discussion

This is the first blinded study to evaluate the feasibility of dehydrated individuals controlling their own intravenous fluid therapy. It suggests that individuals can rely on thirst to manage parenteral rehydration. The group mean thirst score at each assessment point was closely related to the group mean pOsm (within-subject r = 0.74) across both study conditions and throughout the various stages of dehydration and rehydration. This resulted in a proportionate reduction in demand for intravenous fluid as pOsm corrected, and a return to baseline euhydrated body mass in the HV delivery condition. Taken together, this indicates that, where adequate intravenous fluids are available, thirst-guided self-administered fluid allowed individuals to rapidly and accurately rehydrate themselves to a euhydrated state.

Our results demonstrate that thirst may be a reliable guide for fluid intake via a route other than oral. Sensory input from oropharyngeal (peripheral) osmoreceptors (by drinking) helps regulate thirst and fluid intake.[25] It has been suggested that such input, by drinking, is necessary to satiate thirst and to limit excessive fluid intake.[25] We show neither to be true: the HV condition had the potential to self-administer excessive fluid, however fluid administration fell as pOsm reduced, such that the mean volume of fluid demanded (3.06 kg) was not different to the mean body mass loss through dehydration (3.08 kg). The timely responsiveness of thirst to intravenous fluid, demonstrated in this study, is particularly important to mitigate risk of fluid overload.

A recent systematic review and meta-analysis regarding the sensitivity of thirst reported that, across a range of ages and physiological states, there is a pOsm onset threshold of approximately 285 $mOsm.kg^{-1}$.[16] Interestingly, this shows good agreement with our calculated pOsm at which zero demand for fluid would occur. The review further describes that, despite inter-individual variability, the pOsm at which thirst is sensed demonstrates highly consistent intra-individual measures. In addition, thirst intensity displays a linear relationship with increasing pOsm. Our findings support the

conclusion from this systematic review that thirst may be a more sensitive indicator of dehydration than clinical assessment, and as such may be a superior guide for intravenous fluid management. Our findings also support previous pilot work in which we investigated thirst-driven self-administration of intravenous fluid in healthy volunteers, dehydrated through fluid restriction and pharmacological diuresis.[17] Thirst-driven rehydration was more efficacious than a standard clinician-led regime, and demand for fluid reduced in an appropriate fashion as rehydration progressed. However, participants were unblinded to the intervention and this may have affected demand and thirst scoring. We are not aware of any other studies that have investigated this novel concept of rehydration management.

Dehydration is prevalent and represents a major concern for both community- and hospital-based healthcare.[26,27] A recent UK study reported that 37 % of patients (>65 years) were dehydrated on admission to a large acute hospital.[1] The Dehydration Recognition In our Elders (DRIE) cohort study found around 20 % of older people living in long-term care to be dehydrated (serum osmolality >300 $mOsm.kg^{-1}$) and nearly half to be either dehydrated or at risk of becoming so ($\geq$295-300 $mOsm.kg^{-1}$).[3] In 2004, The US National Hospital Discharge Survey reported over 500,000 hospitalisations were primarily due to dehydration, incurring healthcare costs in excess of 5 billion dollars.[2] Furthermore, it has been repeatedly shown that dehydration is associated with increased mortality[1,28–31] and morbidity.[3–8,32] Clinical signs of dehydration are variable and non-specific and there remains no reliable objective diagnostic test with everyday utility.[9,11] As such, hydration status is often ineffectively managed in hospitals, with several studies demonstrating that patients become dehydrated *during* hospital admission.[33–37] There is clearly a great need to improve our methods of assessment and management of dehydration if patient outcomes are to be improved. Thirst-driven patient controlled fluid may represent an appropriate alternative to the current standard of care.

There are several limitations in our study. We only studied male participants, albeit that gender and menstrual cycle phase may have only minor influences on thirst.[16] Dehydration has multiple

aetiologies and represents a heterogeneous group of conditions with varying clinical and biochemical presentations. This study involved participants who had been rendered dehydrated due to the uncompensated, predominantly pure water loss from excessive sweating. As a result, the extracellular fluid (i.e. plasma and interstitial fluid) becomes hypertonic with respect to the intracellular space.[9,38–41] In other circumstances, however, dehydration may result from water deficit that has been accompanied by a proportionate salt loss (e.g. secretory diarrhoea). In this scenario, the extracellular fluid may remain *isotonic* with respect to the intracellular space.[9,38–41] Future studies may, therefore, assess the utility of thirst-driven intravenous fluids in individuals that have been dehydrated through various (patho)physiological processes**.** Secondly, the participants in this study were fit, young and healthy individuals. The degree to which these findings might apply to the clinical environment, where advanced age,[42,43] prescribed medications[44] and comorbidities[45,46] may impact the sensitivity of thirst, is not known. Further research will specifically address this issue.

In conclusion, we accept the hypotheses that the demand for self-administered intravenous fluid in response to thirst is related to the degree of dehydration; that the rate of self-administration reduces in frequency in proportion to the degree of correction of fluid deficit; and that the rate of fluid administration is impacted by the volume of the bolus of fluid administered. Individuals were able to rely on their thirst to appropriately guide demand for fluid intake, irrespective of fluid delivery rate. We have provided proof of concept for participant-controlled, thirst-driven intravenous rehydration therapy. Dehydration remains a major burden in healthcare. Future work must now focus on whether *patient*-controlled intravenous fluids could represent a paradigm shift in the management of hydration in the clinical setting.

Author Contributions

JL, FH, HM and MM conceived the project. JL, JC, FH, MT, MM and HM designed the study. JL, JC, AS, AD, DW were responsible for subject enrolment and data collection. All authors contributed to drafting the manuscript or critically revising it for important intellectual content. All authors approved the final version of the manuscript, and take responsibility for the accuracy and integrity of all aspects of the work.

Declaration of Interests

JL, JC, AS, AD, FH, DW, MT have nothing to declare. HM and MM hold a patent related to patient-controlled hydration [patent number EP2525767B1]. HM consults for Google Health, which has an interest in acute kidney injury. MM consults for Edwards Lifesciences and Baxter. MM is the founding Editor of Perioperative Medicine, sits on the Editorial Boards of The British Journal of Anaesthesia and Critical Care, and is founding Editor-in-Chief of TopMedTalk.

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Figures

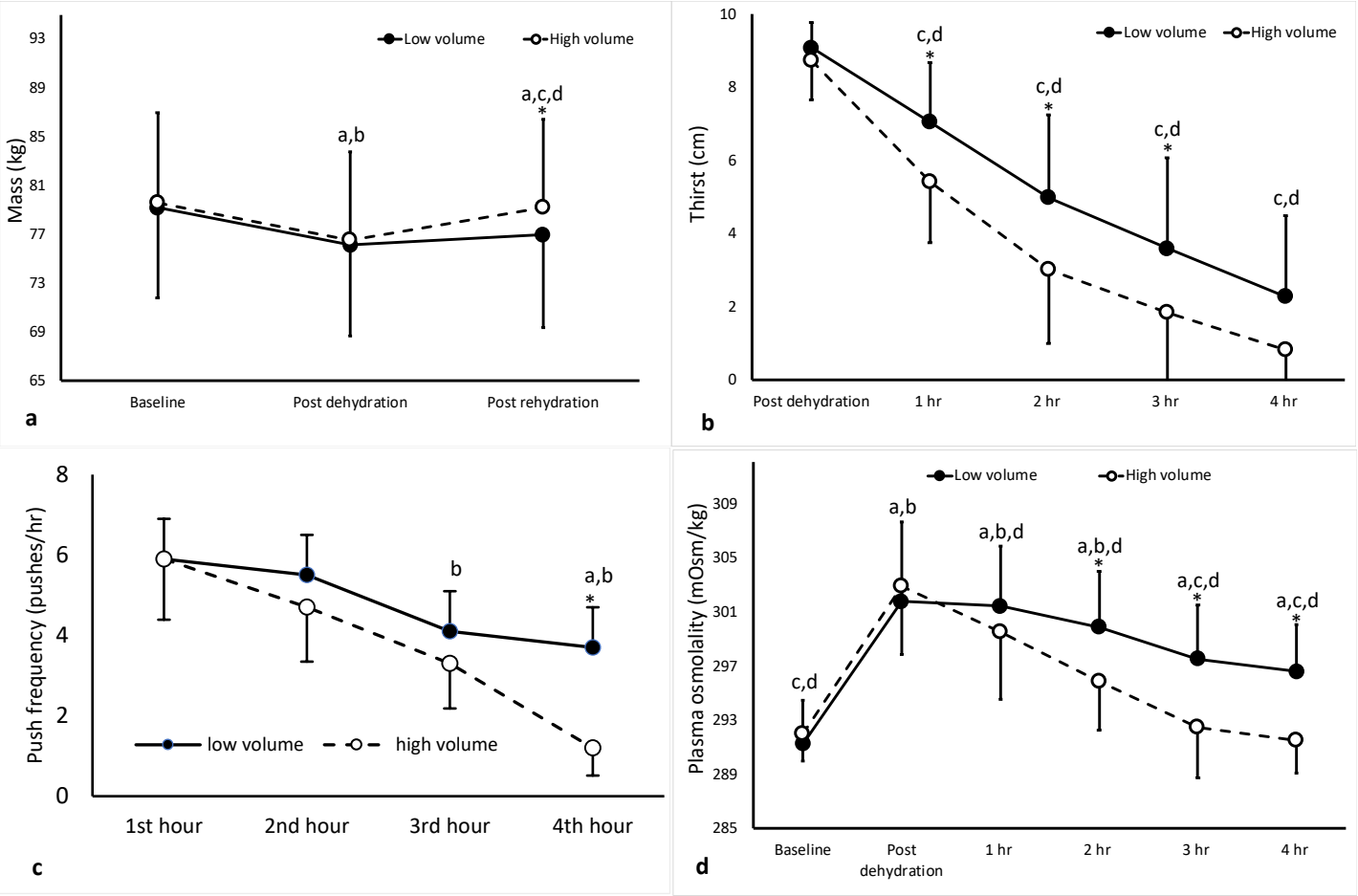

Figure 1a: Mean(SD) body mass at baseline, following the dehydration intervention and following the rehydration intervention, for low and high volume conditions. * = between conditions difference, P<0.05. a = low volume group different from baseline; b = high volume group different from baseline; c = low volume group different from post dehydration; d = high volume group different from post dehydration. **1b:** Mean(SD) thirst scores following the dehydration phase and over the course of the rehydration phase of the experiment, for low and high volume conditions. * = between conditions difference, P<0.05. c = low volume group different from post dehydration; d = high volume group different from post dehydration. **1c:** Push frequency (95% CI) over the course of the rehydration phase of the experiment, for low and high volume conditions. * = between conditions difference, P<0.05. a = low volume group different from 1st hour; b = high volume group different from 1st hour. **1d:** Mean(SD) pOsm data at baseline, and following the dehydration and rehydration phases of the protocol, for low and high volume conditions. * = between conditions difference, P<0.05. a = low volume group different from baseline; b = high volume group different from baseline; c = low volume group different from post dehydration; d = high volume group different from post dehydration.

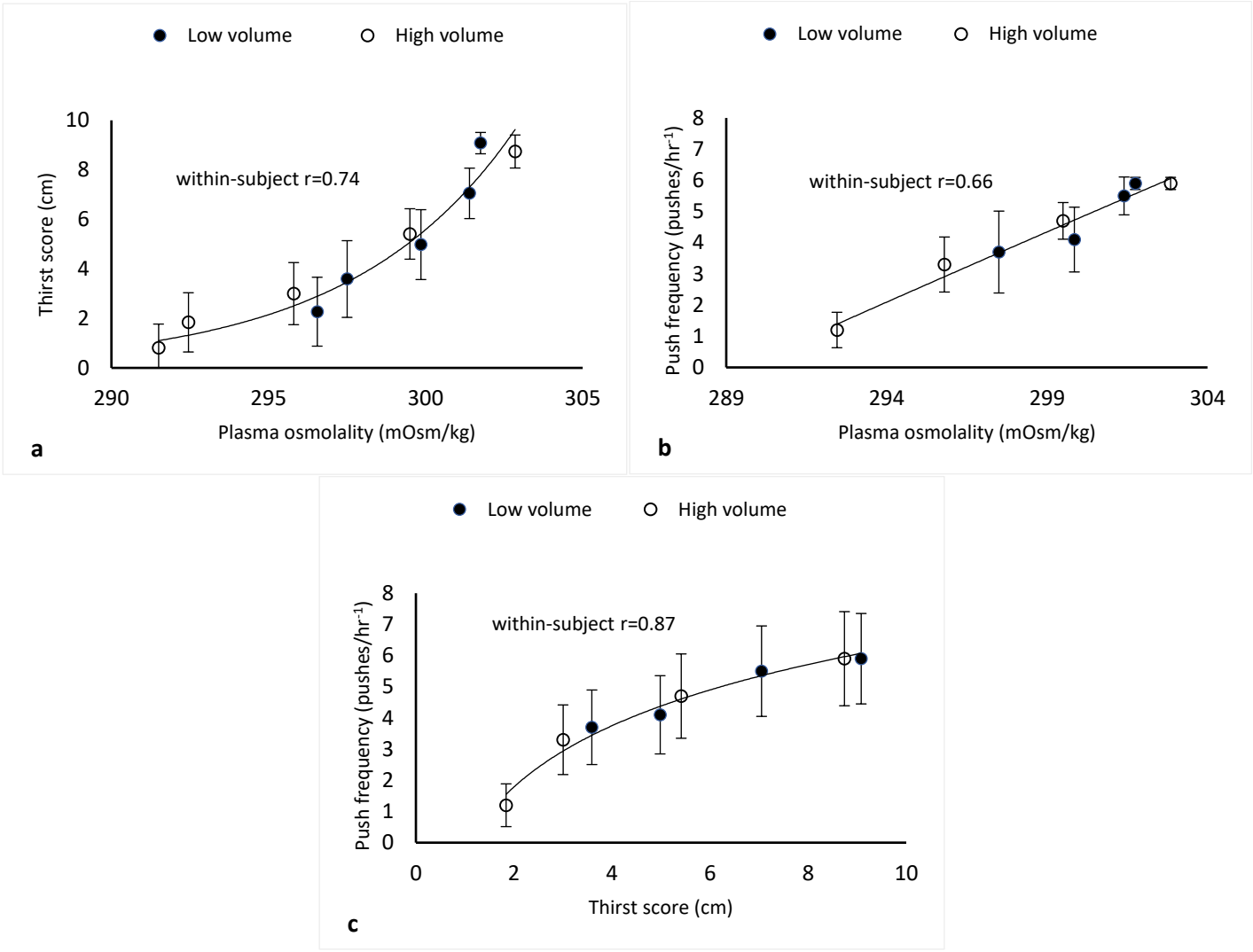

Figure 2a: Mean pOsm (95% CI) following the dehydration phase and for each hour of the rehydration phase, versus mean thirst score for low and high volume conditions. **2b**: Mean pOsm (95% CI) following the dehydration phase and for each hour of the rehydration phase, versus median push frequency for low and high volume conditions. **2c:** Mean thirst score (95% CI) following the dehydration phase and for each hour of the rehydration phase, versus median push frequency, for low and high volume conditions.