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Title: Electrolyte beverage consumption alters electrically induced cramping threshold

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Electrolyte beverage consumption alters electrically induced cramping threshold

Introduction: Recent investigations have questioned the role of hydration and electrolytes in cramp susceptibility and thus the efficacy of consuming electrolyte-rich beverages (EB) to control/prevent cramping. **Methods**: Nine euhydrated, cramp-prone participants had their cramp susceptibility assessed by measuring the nerve stimulation threshold frequency at which cramping occurs (TF) before and after consumption of an EB (kCal: 120, Na: 840 mg, K: 320 mg, Mg: 5 mg) and placebo beverage (PB: kCal: 5, Na: 35 mg). Cramp intensity was assessed using a verbal pain scale and post-stimulation electromyography (EMG). **Results**: TF was greater in EB (14.86±7.47 hz) than PB (14.00±5.03 hz, p=0.038) and reported pain was lower in EB (2.0±0.6) than PB (2.7±0.8, p=0.025) while EMG was similar (p=0.646). **Discussion**: EB consumption decreased cramp susceptibility and pain but did not prevent cramping in any participants. These results suggest that electrolyte consumption independent of hydration can influence cramp susceptibility in young people.

Key Words: Cramp, hydration, body water, sports drink, sodium

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Introduction

Exercise associated muscle cramps (EAMC) are characterized by painful, involuntary muscle contractions during or after fatiguing exercise (1) and are common in both endurance events (2,3) and team sports (4). The etiology of EAMC has been credited to altered hydration and electrolyte balance stemming from sweat induced sodium loss (5,6,7) and altered neurological function related to fatigue. Thus, electrolyte-rich carbohydrate beverages (EB) have the potential to increase EAMC resilience by offsetting fluid and electrolyte losses and decreasing glycolytic fatigue associated with high intensity exercise. It has been shown that consuming a sodium supplemented carbohydrate beverage in hot environments prior to exercise more than doubles time to cramping compared to no fluid consumption (8), but does not completely prevent cramping from occurring, as ~70% of participants still experienced cramping (8).

Several studies have challenged the role that hydration and electrolyte balance have in EAMC by observing that dehydration and serum electrolyte changes during ultra-endurance events were not predictive of runners who experienced EAMC during the race (9,10). Rather EAMC was exclusively related to personal cramp history and running intensity (9,10). These results suggest that hydration and electrolyte balance are not the sole contributors to EAMC and their effects on EAMC susceptibility should be investigated using controlled within subject experiments. There is presently no valid and reliable within subject experimental model to test EAMC susceptibility

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in the conditions in which they are most likely to occur. Alternatively, the nerve stimulation cramp threshold frequency (TF) at which a cramp occurs has been shown to be a valid and reliable measure of EAMC cramp susceptibility (13,14). When using the TF model it was found that hypohydration did not significantly affect TF (11,12), however, it was also observed that TF increased on average 1.8 Hz after consumption of pickle juice compared to deionized water in hypohydrated participants, supporting consumption of an electrolyte rich beverage to increase cramp resiliency (15).

While EB are widely available and commonly consumed during exercise, there is still no well-controlled, randomized study that has determined if commercially available EB can decrease cramp susceptibility in euhydrated individuals. Thus, the purpose of the present study is to determine if EB consumption alters the frequency of nerve stimulation at which a cramp occurs (TF) compared to a placebo beverage (PB) with similar fluid volume and flavor profile. We hypothesize that EB consumption will increase TF, indicating greater cramp resilience when compared to PB consumption.

Methods

This study was a randomized controlled trial with a repeated measures and crossover design (see Supplemental Figure 1). Each participant was considered cramp prone, which was defined in

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this study as self-reporting experiencing EAMC of the triceps surae on a regular basis (at least monthly). At the time of testing, participants reported that they were free from any musculoskeletal injury or any cardiovascular, neuromuscular or neurological disease as determined by a medical health history questionnaire. The institutional review board at the University of Rhode Island approved this study and all participants provided written informed consent prior to participation.

Each participant took part in a screening session used to familiarize them with the experimental methods and ensure that a flexor hallucis brevis cramp could be elicited using electrical stimulation. Participants also completed two experimental sessions, each separated by a 1-week washout period (14). During the experimental sessions, participants had TF of the flexor hallucis brevis measured after consumption of an electrolyte-rich carbohydrate beverage (EB) or a control beverage (PB). When a cramp occurred, muscle activity of the flexor halluces brevis (EMG) was recorded and participants reported the pain experienced during cramping using the verbal pain scale (VPS) (17). The order of the treatments was randomized and counterbalanced and participants were blinded to treatment.

Each testing session was performed at the same time of day (± 0.5 h). Prior to testing sessions participants confirmed they abstained from strenuous physical activity for at least 24 h, alcohol or other depressants for at least 12 h, and caffeine or other stimulants for at least 6 h.

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Additionally, diet was assessed using a 24 h diet recall. Diet records were analyzed for calorie and electrolyte consumption using diet analysis software (ASA24, National Institute of Health, USA). Participants were also instructed to attend sessions euhydrated, which was confirmed as a urine specific gravity ≤ 1.020 (18). Hydration and fluid distribution were assessed via a multi-frequency bioelectrical impedance test (InBody 770, InBody, Cerritos USA: 19).

After hydration status was assessed and euhydration confirmed, participants had the skin over the medial gastrocnemius and flexor hallucis brevis shaved, abraded, and cleaned with alcohol before being outfitted with 1 cm^2 parallel bar wireless EMG electrodes (Trigno IM, Delsys, Natic, USA) over each muscle. Raw EMG signals along with nerve stimulator output signals were recorded by a data acquisition system (PowerLab, AD Instruments, Colorado Springs USA) at a rate of 2000 Hz and displayed to the participant in real time using associated software (LabChart Pro, AD Instruments, Colorado Springs USA). Raw flexor hallucis brevis and medial gastrocnemius signals were used for biofeedback in order to minimize contribution of the plantar flexors during great toe flexion exercise. Flexor hallucis brevis signals were filtered using a Butterworth, 2^{nd} order 10-500 Hz band-pass filter and reported as a percentage of activity in reference to a maximal voluntary isometric contraction (MVIC). Root mean square of EMG was calculated at rest (1 s), during the MVIC (1 s), and 2 s after the start of the cramp. EMG during cramping was used to assess cramp intensity and was reported as a percentage of MVIC (20).

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After EMG set-up, the participant was instructed to lay supine on a plinth with their left foot in a custom-built rigging that positioned their ankle to 120° plantar flexion with their heel and forefoot resting upon a board, and their great toe placed upon a calibrated load cell (see Supplemental Figure 2). Nylon straps were used to secure the thigh to a plinth and both nylon and elastic straps were used to secure the leg and foot to the rigging. To prime the nervous system and elicit mild fatigue, participants performed 15, 2 s great toe flexion MVIC's each separated by 1 min (15). Afterward, participants were given 5 min of rest followed by 3 additional MVIC's each separated by 1 min. Of these 3 MVIC's, the repetition with the greatest 500 ms root mean square window was then used to normalize EMG during cramping.

Once the final MVIC was completed participants were given 0.5 L of their assigned beverage for consumption. Both beverages were similar volume (0.5 L), color and general flavor (lemonade), and mixed with the same brand of bottled water. The EB was a commercially available beverage packet (Fuelocity Plus, United Citrus Corp, Norwood USA) with 120 kCals, 29 g of sugar, 840 mg of sodium, 320 mg of potassium and 5 mg of magnesium and 300 mg of l-alanine, while the PB was a commercially available low-calorie beverage packet (Crystal Light, Kraft Foods Inc., Northfield USA) with 5 kCals, 0 g of sugar, 35 mg of sodium and 0 mg of potassium, magnesium and l-alanine.

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Participants were given up to 5 min to consume their assigned beverage and were then given 15 min prior to the start of TF testing. These durations were selected as they are believed to be similar to those that an athlete may adopt before competition or a conditioning session. During this time, a round 8 mm (diameter) Ag-AgCl stimulating electrode was placed over the tibial nerve slightly inferior to the medial malleolus, which sent a dispersing electrical stimulus to an 8 cm^2 sponge electrode placed directly over the lateral malleus (20). To ensure proper placement of the electrode the tibial nerve was submaximally stimulated up to three times with an 80 V, 2 ms pulse to ensure strong flexion of the great toe (Grass S88, Astro-Med Inc West Warwick RI, USA). When positioning was confirmed, electrodes were anchored in place using medical and elastic tape.

To determine TF, participants had their tibial nerve stimulated with an 80 V biphasic 2 s train at increasing frequencies until a cramp occurred. The starting frequency for each participant was 8 Hz, and the frequency increased by 2 Hz every minute until a cramp occurred. Participants who did not cramp after their 12^{th} stimulation (30 Hz) were excluded from the study, as these participants were determined to not be cramp sensitive. Three criteria were required to be met for a muscle cramp to be confirmed: 1) the participant confirmed that they experienced an involuntary sustained contraction after the cessation of the stimulus, 2) the researcher used load cell data to confirm that involuntary contraction of the flexor hallucis brevis occurred, and 3) the EMG average root mean square for the 2 s after the cessation of the stimulation had to be greater

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than the mean plus 2 standard deviations of the raw baseline EMG measurement (20). Upon the initiation of a cramp, participants were given 10 s for the cramp to naturally dissipate. During this time participants remained with their body, foot and toe strapped into position. After 10 s participants were rapidly unstrapped and they were permitted to stretch and/or massage the toe. Using this method, cramps were reliably induced in both conditions (inter-day ICC = 0.908).

Immediately after this 10 s period participants were presented with a 6-point VPS, where 1 = No Pain, 2 = Mild Pain, 3 = Moderate Pain, 4 = Severe Pain, 5 = Very Severe Pain, and 6 = Worst Pain Possible (17).

All results are reported as means and standard deviations. Differences between the two beverages in TF and EMG were determined using a paired t-test and differences in VSP were determined using a Wilcoxon Signed Rank test. For both tests the accepted α level of 0.05 was used. Cohen's D effect sizes are reported from delta values. An a-priori power analysis revealed that sample size (n = 9) of the present study was appropriate to test for a very large effect (Cohen's D = 1.2), which was deemed a clinically significant effect, at a power of 0.85 and accepted alpha of 0.05 using G-Power (Version 3.1, Dusseldorf Germany). Statistical analysis was performed using SPSS (Version 24, IBM, Armonk USA).

Results

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Twelve cramp prone participants were recruited and took part in a screening session. Of these participants, three were excluded from the study, as we were unable to successfully induce a cramp by the 12th incremental nerve stimulation (30 Hz). This resulted in nine participants (7 male & 2 female, age: 23.6 ± 4.2 y, height: 175.4 ± 16.0 cm, mass: 71.2 ± 9.3 kg, body composition: 15.5 ± 9.0% fat) who completed this study. In addition to regularly experiencing EAMC in their triceps surae, a subset of the cohort also reported regularly experiencing cramps in the foot or toes (n=5), abdominals (n=2), triceps brachii (n=1) and hamstrings (n=1). EAMC were reported to occur during running (n=5), soccer (n=2), basketball (n=2), lacrosse (n=1), resistance training (n=1) and during the recovery period immediately after intense exercise (n=4). In addition to regularly experiencing EAMC, four participants also reported experiencing spontaneous cramping while sleeping.

When comparing of hydration and fluid distribution prior to cramp testing it was found that participants had similar urine specific gravity (EB: 1.0119 ± 0.0056, PB: 1.0109 ± 0.00541, item mean range 0.001) and total body- (EB: 43.4 ± 8.5 kg, PB: 43.9 ± 9.1 kg,,ICC = 0.996, $p < 0.001$), intercellular- (EB: 26.8 ± 7.3 kg, PB 27.7 ± 5.9 kg; ICC = 0.916, $p = 0.001$), extracellular-water (EB: 16.3 ± 2.0 kg, PB: 16.2 ± 2.2 kg; ICC = 0.997, $p < 0.001$), and extracellular-water to total body-water ratio (ICC = 0.978, $p < 0.001$) between conditions.

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Analyzed 24 h diet recall revealed calorie, macronutrient and electrolyte consumption did not differ between conditions as indicated by non-significant paired t-tests ($p = 0.219 – 0.673$). Furthermore, electrolyte consumption of potassium (EB: 1377 ± 459, PB: 1547 ± 516 mg; ICC = 0.755, $p = 0.038$), and magnesium (EB: 233 ± 78, PB: 209 ± 70 mg; ICC = 0.799, $p = 0.017$) were similar between conditions. However, while not different ($p = 0.219$) consumed sodium was not statistically similar between conditions (EB: 1737 ± 579, PB: 1679 ± 560 mg; ICC = 0.685, $p = 0.058$).

Grouped and individual results from cramp testing are reported in Table 1 and Figures 1 & 2 respectively. In the present study, TF was found to be a reliable measure of cramp sensitivity (inter-day reliability: ICC = 0.908). Results demonstrated that TF was significantly higher in EB compared to PB. Compared to the PB, 5 of 9 participants required a greater stimulation frequency to elicit a cramp after consumption of the EB, while the remaining 4 participants had the cramp occur at the same stimulus frequency. Participants reported experiencing significantly greater pain in the PB (Median = Moderate Pain) compared to the EB (Median = Mild Pain) condition when using the verbal pain scale, with 6 of 9 participants reporting less pain in the EB condition and the remaining 3 participants experiencing similar pain. EMG was similar between conditions, with 5 of 9 participants experiencing greater muscle activity after consumption of the EB compared to the PB and 4 of 9 experiencing less muscle activity.

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To determine if an order effect was present, a separate repeated measures ANOVA with Bonferoni correction was used to compare TF between the screening session (13.3 ± 7.1) and the first (12.4 ± 4.9) and second (11.3 ± 4.2) experimental sessions. From this analysis no difference was observed between the screening session and the first experimental session ($p = 1.000$) or between the first and second experimental session ($p = 0.536$).

To determine if participant condition blinding was effective each participant completed an exit survey asking which session they believe they received the EB and PB conditions. In this survey 4 of 9 participants incorrectly guessed their conditions.

Discussion

The primary finding of the present study was that consumption of an EB resulted in a statistically large increase in TF compared to the consumption of a similarly flavored PB in euhydrated participants. These results indicate that participants required a greater electrical stimulus frequency to elicit a muscle cramp after consumption of the EB, which suggests that EB consumption independent of hydration can decrease cramp susceptibility in young people. While this is a statistically significant difference with a large effect size, the clinical applicability of this change in TF remains unknown, as no minimal detectable change in TF is established in the literature. Additionally, as 4 of the 9 euhydrated cramp prone participants experienced no

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difference in TF between conditions, it is possible that either the effect size of the EB was smaller than the resolution (Δ2 Hz) of the test or that in these participants there was no effect of beverage on TF. However, the observed difference between conditions of 1.56 Hz is comparable to differences observed when comparing pickle juice to deionized water (1.8 Hz) (15) and TRPV1 & TRPA1 activators (motor neuron inhibitors) to gelatin gel capsules (1.1 Hz) (16).

Sports drinks, such as the EB used in the present study, have the potential to decrease cramp susceptibility by maintaining fluid and electrolyte homeostasis as a result of the water and electrolyte components, and may increase energy availability during intense exercise, both of which may prevent fatigue. However, the present study design allows for general fluid consumption to be dismissed as a potential mechanism by which TF increased because participants 1) attended each session euhydrated (urine specific gravity ≤ 1.020), 2) had similar hydrations and fluid distribution measures in both testing sessions, and 3) consumed beverages with similar volumes. These results suggest that the proprietary non-water ingredients of the EB accounted for the differences in TF observed presently. However, while general fluid consumption was matched between conditions it could be reasonable to assume that absorption of the water 15 min post-consumption was greater in the EB condition than PB condition at this time due to the non-water ingredients of the EB.

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While the effect of the carbohydrate component of the EB on TF cannot be discounted, we believe that an effect is unlikely as the exercise performed as the conditioning activity (2 s isometric contractions with 1 min inter-contraction rest) would suggest that there is minimal contribution of glycolytic metabolism (22). However, as carbohydrate mouth rinses have been shown to result in altered exercise performance and brain activity that is independent of gastrointestinal absorption, it is possible that carbohydrate within the EB may have resulted in an altered neural signaling which may have effected TF (23).

Another factor which could influence TF is the beverage flavor. After the observation that TF was greater after consumption of pickle juice compared to deionized water, it has been suggested that differences between conditions may have results from an oropharyngeal-region neurally mediated reflex (15). Although pickle juice has a distinct and contrasting taste compared to deioniozed water, the present study utilized two beverages with similar flavor profiles to account for a placebo effect and the general effects of flavoring on TF. However, this does not fully account for oropharyngeal-region reflexes as it was impossible to identically match flavor between beverages and in our exit survey only 4 of 9 participants incorrectly guessed which condition they received on which day. Therefore it is possible that participant blinding was not completely effective.

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A secondary finding of the present study was that pain was significantly lower in the EB compared to the PB condition, with each participant reporting less (6 of 9) or similar (3 of 9) pain after consumption of the EB. While significantly less pain was experienced in the EB than PB group, EB also received greater electrical stimulus frequency, therefore the effect sizes reported for VPS likely underrepresent the true effect of EB on pain (20-21). Unlike pain, relative muscle activity did not significantly differ between conditions. These results suggest that the cramping muscle was similarly active between conditions. However, several studies have questioned the use of surface EMG during cramp measurements, as muscle cramp is characterized by spatially inconsistent muscle activation and significant intramuscular cross talk in the flexor halluces brevis (24).

While the results from the present study may be of great interest to those who often treat or experience EAMC it is important to note the following limitations to the study design. Firstly, while strongly related to incidence rate of EAMC, repetitive nerve stimulation does not necessarily incorporate all the factors related to EAMC. Secondly, intramuscular and skin temperature were not measured and these variables may affect cramp sensitivity. Thirdly, the homogenous age of the study participants leaves the question as to whether these results would be similar in younger or older cohorts. Additionally, the present study used a single blinded design rather than a double-blinded design. Finally, while all participants reported they did not

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have any underling etiology that would predispose them to secondary cramping, it cannot be definitively stated that no such conditions were present in our sample.

Overall, the results of the present study found that EB can increase the electrical stimulus frequency required to elicit a cramp (TF) and decrease the pain experienced when a cramp occurred in euhydrated, cramp prone individuals. However, EB did not prevent cramps from occurring in any participants. Additionally, the study design used supports the notion that the electrolytes contained within the EB are responsible for such differences, however differences due to beverage flavoring and carbohydrates cannot be fully discounted. As TF is related to an individual's susceptibility to EAMC (13) these results provide support for the efficacy EB for increasing resistance to EAMC. However, more research is needed to explore the relationship between electrically induced (TF) and exercise associated (EAMC) muscle cramping as well as to define a clinically significant change in TF.

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Abbreviations:

CB: Control beverage

EAMC: Exercise associated muscle cramp

EB: Electrolyte-rich beverage

EMG: Electromyography

TF: Threshold frequency at which muscle cramp occurs

VPS: Verbal pain scale

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Figure Legends

Figure 1: Individual responses to consumption of an electrolyte rich beverage (EB) and placebo beverage (PB) on cramp threshold frequency (TF) and electromyography (EMG) during electrically induced cramps. Participant numbers (1-9) are provided in spaces next to each measurement.

Figure 2: Grouped (left) and individual (right) responses to consumption of an electrolyte rich beverage (EB) and placebo beverage (PB) on reported pain during electrically induced cramps using a verbal pain scale (VPS). Participant numbers (1-9) are provided in spaces next to each measurement.

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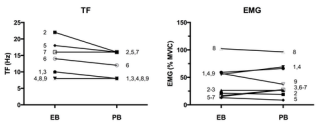

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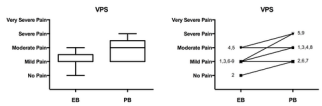

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Table 1 – Comparison between testing conditions

	PB	EB	p	95% CI	Effect Size
TF (Hz)	11.11 ± 3.89	12.67 ± 5.10	0.043*	0.06 to 3.05	0.800
Pain (VPS)	2.88 ± 0.84	2.00 ± 0.54	0.006*	-1.41 to -0.34	1.365
EMG (%MVIC)	46.2 ± 22.2	44.1 ± 19.8	0.724	-9.6 to 7.0	0.122
USG	1.0109 ± 0.006	1.0119 ± 0.005	0.600	-0.003 to 0.005	0.194

TF: cramp threshold frequency, VPS: verbal pain scale, EMG: electromyography, USG: urine specific gravity, EB: electrolyte rich beverage, PB: Placebo beverage

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