Reflex Inhibition of Electrically Induced Muscle Cramps in Hypohydrated Humans

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ABSTRACT

MILLER, K. C., G. W. MACK, K. L. KNIGHT, J. T. HOPKINS, D. O. DRAPER, P. J. FIELDS, and I. HUNTER. Reflex Inhibition of Electrically Induced Muscle Cramps in Hypohydrated Humans. *Med. Sci. Sports Exerc.*, Vol. 42, No. 5, pp. 953–961, 2010. **Introduction**: Anecdotal evidence suggests that ingesting small volumes of pickle juice relieves muscle cramps within 35 s of ingestion. No experimental evidence exists supporting the ingestion of pickle juice as a treatment for skeletal muscle cramps. **Methods**: On two different days (1 wk apart), muscle cramps were induced in the flexor hallucis brevis (FHB) of hypohydrated male subjects (~3% body weight loss and plasma osmolality ~295 mOsm·kg^{-1} H_2O) via percutaneous tibial nerve stimulation. Thirty minutes later, a second FHB muscle cramp was induced and was followed immediately by the ingestion of 1 mL·kg^{-1} body weight of deionized water or pickle juice (73.9 ± 2.8 mL). **Results**: Cramp duration and FHB EMG activity during the cramp were quantified, as well as the change in plasma constituents. Cramp duration (water = 151.9 ± 12.9 s and pickle juice = 153.2 ± 23.7 s) and FHB EMG activity (water = 60% ± 6% and pickle juice = 68% ± 9% of maximum voluntary isometric contraction EMG activity) were similar during the initial cramp induction without fluid ingestion ($P > 0.05$). During FHB muscle cramp induction combined with fluid ingestion, FHB EMG activity was again similar (water = 55% ± 9% and pickle juice = 66% ± 9% of maximum voluntary isometric contraction EMG activity, $P > 0.05$). However, cramp duration was 49.1 ± 14.6 s shorter after pickle juice ingestion than water (84.6 ± 18.5 vs 133.7 ± 15.9 s, respectively, $P < 0.05$). The ingestion of water or pickle juice had little impact on plasma composition 5 min after ingestion. **Conclusions**: Pickle juice, and not deionized water, inhibits electrically induced muscle cramps in hypohydrated humans. This effect could not be explained by rapid restoration of body fluids or electrolytes. We suspect that the rapid inhibition of the electrically induced cramps reflects a neurally mediated reflex that originates in the oropharyngeal region and acts to inhibit the firing of alpha motor neurons of the cramping muscle. **Key Words:** ACETIC ACID, DEHYDRATION, ELECTROLYTES, PICKLE JUICE, VINEGAR

Skeletal muscle cramps that occur during or shortly after exercise have been termed exercise-associated muscle cramps (EAMC). These muscle cramps are highly prevalent in athletic populations (3,8,36) and the physically active (25). In fact, 73% (102/139) of heat-related injuries experienced in American football were EAMC (8). In triathletes, 67% (1631/2438) complained of EAMC under a variety of training conditions (14). Despite their prevalence, the etiology of EAMC is unclear.

Traditionally, EAMC have been associated with fluid and electrolyte disturbances (6,32,35). Proponents of this theory hypothesize that the loss of fluids and electrolytes owing to exercise-induced sweating causes a contracture of the interstitial space, which results in mechanical deformation of nerve endings and leads to cramp genesis (4,16). This theory is based on the observation that athletes who develop EAMC often have significant fluid and electrolyte losses at the time of cramp (3,32). However, losses in plasma and blood volume, electrolytes, and body weight are often similar in individuals who develop EAMC as in noncramping individuals (18,30). In addition, EAMC can be relieved by moderate static stretching of the cramping muscles (17,30,35) or activation of Golgi tendon organs (15). Neither of these treatment strategies has any impact on fluid or electrolyte balance, yet both adequately relieve a skeletal muscle cramp.

The unclear etiology and conflicting results of observational studies regarding EAMC have resulted in several anecdotal treatments, many with little or no scientific credibility. One such treatment is the ingestion of small volumes (30–60 mL) of pickle juice, a highly salty and acidic brine. This treatment is claimed to relieve an EAMC within 35 s (38). Several athletic trainers (25%, 92/370) seem to be

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treating athletes who develop EAMC with pickle juice (22) despite the lack of scientific evidence of its efficacy and the warnings against its ingestion (10). Many of these health professionals attribute pickle juice's efficacy to the high sodium (Na^+) and electrolyte content (22).

We examined whether pickle juice could relieve an electrically induced muscle cramp in mildly hypohydrated humans by inducing skeletal muscle cramps with low-frequency percutaneous electrical stimulation. The ability to initiate a cramp via low-frequency activation of the alpha motor neuron (5,34) supports the hypothesis that the muscle cramp is generated peripherally, either at the level of the alpha motor neuron or motor end plate (24). This cramp induction model effectively induces skeletal muscle cramps and is generally well tolerated and reliable and has a close correlation with the occurrence of EAMC (21,33).

If pickle juice relieves an electrically induced muscle cramp, we questioned how quickly it relieved the muscle cramp and if the cessation of the cramp was associated with a change in plasma electrolyte concentration or other plasma constituents. We hypothesized that pickle juice would alleviate an electrically induced muscle cramp but that this effect would not occur within 35 s of ingestion. In addition, we did not expect any appreciable changes in plasma constituents within 5 min after ingestion.

METHODS

Subjects. Twelve healthy, unacclimated college-aged males volunteered for this study. Two volunteers were excluded from participating because we could not induce a cramp on the first day of testing. Therefore, 10 subjects (mean ± SE, age = 23.5 ± 1.0 yr, height = 177.8 ± 1.8 cm, mass = 73.9 ± 2.8 kg) completed the study. Volunteers were excluded from participating if they 1) had experienced any lower extremity injury or surgery within the last 6 months or 2) self-reported any neurological, cardiovascular, or blood-borne diseases. All subjects had experienced EAMC within 6 months of experimentation. All procedures were approved by our university's institutional review board, and subjects provided written informed consent. To protect against a placebo effect, subjects were not informed what they would be drinking or the beverage's purported effects on muscle cramps.

Testing procedures. Subjects reported for a familiarization session and two experimental trials. No data were collected on the familiarization session. This session was used to screen potential subjects to ensure that an electrically induced cramp could be induced in the flexor hallucis brevis (FHB) and that subjects could tolerate the electrical stimuli. The familiarization session occurred 24 h before the first experimental trial for all subjects.

On the familiarization day, subjects were taught how to perform a maximum voluntary isometric contraction (MVIC) with their dominant leg's FHB by performing 15 practice MVIC. Each 2-s MVIC was separated by 1 min of rest. After the last practice MVIC, subjects rested for 15 min, and we attempted to induce a cramp in the FHB via low-frequency percutaneous electrical stimulation of the tibial nerve. If successful (see criteria in the next paragraph), EMG and stimulating electrode placements were marked for replication, and subjects were invited back the following day for the first experimental trial. Subjects were instructed to fast for 12 h before the experimental trials, to drink water consistently throughout the evening and morning before these trials, and to avoid exercising for 24 h before testing.

On the first experimental trial day, subjects reported to the laboratory and were weighed, and a venous catheter was inserted into a superficial vein in the forearm. Subjects ingested 5 mL of tap water per kilogram body weight within 5 min to help ensure hydration and lay supine for 30 min during which they were prepared for several measurements. A portion of the right midforearm was shaved in preparation for sweat patch placement. Subjects' legs were then prepared for EMG analysis using standard preparatory procedures (34). After this equilibration period, subjects voided their bladders completely, and their urine was collected (first urine collection). Subjects were weighed and then lay supine for an additional 30 min after which they practiced performing 15, 2-s MVIC with 1 min of rest separating each contraction. After the last practice MVIC, subjects rested for 5 min and then performed three consecutive 2-s MVIC. The mean EMG activity (V) of these MVIC was recorded and averaged for statistical analysis. After 15 min of rest, subjects voided their bladders (second urine collection) and were weighed.

An HR monitor was placed on the chest (Polar Electro, Inc., Lake Success, NY). The right forearm was washed with distilled water and dried. A sterile sweat patch was placed on the forearm. Subjects then began a 30-min bout of one-leg (nondominant), semirecumbent cycle ergometer exercise at 41°C and 15% relative humidity. Subjects exercised at a moderate intensity that generated an HR between 145 and 150 bpm. After 30 min of exercise, subjects were towel-dried, weighed, and rested for 5 min. This cycle of 30-min exercise/5 min rest continued until subjects lost ~3% of their body mass (2.1 ± 0.1 h). None of our subjects experienced EAMC as a result of the exercise protocol.

When subjects became sufficiently hypohydrated, they exited the heat chamber, voided their bladders (third urine collection), and lay supine on a treatment table for 30 min to allow body fluid compartment equilibration. Subjects' MVIC EMG activity was reassessed. A cramp in the FHB was induced, and cramp duration and FHB EMG activity were recorded. No fluids were ingested during this cramp. Subjects were instructed to remain relaxed for the duration of the cramp and to let the cramp proceed for as long as possible. On cramp cessation, subjects voided their bladders (fourth urine collection).

Subjects lay supine for 30 min after cramp induction after which we collected a 5-mL blood sample (baseline). Subjects then sat up slightly to facilitate fluid ingestion. The

primary investigator and subject donned nose plugs to prevent discovery of the drink composition. Subjects were instructed to allow the upcoming cramp to persist as long as possible, not make any sounds, gestures, or facial expressions after fluid ingestion, which may have notified the primary investigator of the contents of the water bottle, and to wait until signaled to ingest the treatment fluid. A cramp was then induced at the same frequency and parameters that had been used to induce the first cramp (e.g., stimulation frequency, intensity). The primary investigator verified cramping (2 s after cramp induction) and then signaled to the subjects to ingest 1 $mL \cdot kg^{-1}$ body weight of either pickle juice or deionized water. They drank the fluid as quickly as possible (3–5 s). At 1 and 5 min after ingestion, 5-mL blood samples were collected. After collection of the last blood sample, subjects voided their bladders (fifth urine collection) and were excused. Each subject completed two identical experimental trials separated by at least 1 wk. The two trials differed only by the composition of the fluid ingested during the electrically induced muscle cramp: pickle juice or deionized water. No other fluids were ingested at any other point by the subjects during experimentation.

Subjects were instructed to not drastically alter their diet and activity level the week in between experimental trials and to remark the locations of the EMG and stimulating electrodes if they noticed the marks were fading during the course of the week. Compliance of these instructions was assessed via a diet/exercise log on the final day of testing.

We collected the pickle juice by straining it from commercially available sliced dill pickles (Vlasic Pickles, Pinnacle Foods Corp., Cherry Hill, NJ). Both treatment fluids were kept in sealed, unmarked, opaque containers and chilled in a refrigerator at 3°C until needed. A research assistant prepared each drink after the first body weight measurement, so both the subject and primary investigator were blinded to its contents. Drink order was randomized and counterbalanced.

Muscle cramp induction and determination criteria. Skeletal muscle cramps induced with this low-frequency, percutaneous electrical stimulation model have both high intrasession (intraclass correlation coefficients (ICC) [3,1] > 0.844) (34) and intersession reliability (ICC [3,1] > 0.963) (20,34). Scientists have used this model to investigate the effects of various interventions (31,40) as well as their correlation with EAMC (21,33).

Subjects lay supine with their dominant ankle hanging off a table and were instructed to relax for the duration of testing. Standard EMG preparatory procedures (34) were performed at the medial plantar aspect of the foot, at the area around the medial malleolus, and at the ipsilateral tibial tuberosity. An 8-mm Ag–AgCl stimulating electrode was placed slightly inferior to the medial malleolus. The tibial nerve was submaximally stimulated two to four times with 1-ms electrical stimuli at 80 V to determine the site around the medial malleolus that caused the greatest hallux flexion. An 8-cm square dispersive electrode was placed over the lateral malleolus. Electrodes were secured with medical tape and an elastic wrap at these locations. Two EMG measurement electrodes were placed 2 cm apart over the midbelly of the FHB with a single-ground measurement electrode over the ipsilateral tibial tuberosity.

The compound muscle action potentials of the FHB were sampled at 2000 Hz and filtered (band-pass low-frequency = 10 Hz and high-frequency = 500 Hz) using the MP150 analog-to-digital system and operated by AcqKnowledge v3.7.3 software (Biopac Systems, Santa Barbara, CA). Disposable long-term recording electrodes (EL502-10; Biopac) were used to collect EMG data. The total EMG recording consisted of baseline (1 s), stimulation (2 s), and poststimulus activity (5 min).

A Grass S88 stimulator with SIU5 Stimulus Isolation Unit (Astro-Med, Inc., West Warwick, RI) with an 8-mm Ag–AgCl shielded active electrode (EL258S; Biopac) and an 8-cm square dispersive electrode was used to deliver the train of electrical stimuli to the tibial nerve. Stimulus intensity and duration were set at 80 V and 2 s, respectively, because this intensity and duration have been shown to induce muscle cramps in healthy subjects (20). Subjects received two consecutive trains of electrical stimuli (one train per second; no rest intervals between trains) beginning at a train frequency of 4 Hz (eight total stimuli on the first trial). If a cramp did not occur at 4 Hz, subjects rested for 1 min, and train frequency was increased by 2 Hz. This process continued until the FHB cramped.

A muscle cramp was defined as an involuntary painful contraction of the FHB immediately after stimulation and was verified by involuntary sustained great toe flexion, subject verification that a cramp had occurred, and an average EMG root mean square amplitude >2 SD above the 1-s baseline EMG average root mean square amplitude (34). Also, induced cramps must have lasted ≥90 s, and cramp intensity must have been approximately 50% of MVIC EMG activity. The stimulation frequency required to induce cramps with the previously mentioned criteria was termed the minimal treatment frequency (MF_{trt}). This is not to be confused with "cramp threshold frequency" that has been reported in previous studies and is defined as the minimal electrical stimulation frequency (Hz) required to elicit mild and short-lasting (i.e., <10 s) cramps (20,21,34).

The FHB EMG activity during each cramp was recorded until it seemed to return to resting activity. The filtered and rectified EMG measurements were saved and placed into an algorithm that calculated cramp duration. Cramps were considered alleviated when the cramp EMG activity was <2 SD above baseline EMG activity. Cramp intensity (%) was calculated by dividing the 2 s of cramp EMG activity immediately after the end of the electrical stimuli by MVIC EMG activity and multiplying by 100.

MVIC EMG activity determination. The dominant legs' big toe was placed in a toe harness that was attached to a strain gauge rated for loads <11 kg and calibrated with

a 4-kg weight. Four-centimeter nylon straps were tightened over the subject's midthigh and shin to prevent movement of the hip and knee. The subject's dominant ankle was placed in a foam block with a foot pad at 120° to keep the ankle in slight plantarflexion and to prevent the ankle from extreme inversion and eversion (Fig. 1). The subjects were instructed to keep the plantar aspect of their foot against this foam block when performing their MVIC. The compound muscle action potentials of the FHB during MVIC were sampled using similar parameters as described above for FHB cramps.

Gastrocnemius muscle activity was monitored with a biofeedback unit (Pathway TR-10C; Prometheus Group, Dover, NH) to ensure that the subjects were not producing force by using the incorrect muscles. Gastrocnemius EMG activity exceeding 8 mV constituted a failed MVIC attempt. If subjects performed an MVIC incorrectly, they rested for 1 min and then reattempted the contraction. These settings have been used successfully in previous experiments (unpublished observations).

Blood analysis procedures. Five-milliliter blood samples were collected before and at 1 and 5 min after ingestion of each fluid. One milliliter of blood from each sample was used to analyze hematocrit (Hct) and hemoglobin (Hb; 0.5 mL for each); the 4 mL of blood remaining was sealed and stored in a 6.0-mL lithium heparin vacutainer (BD, Franklin Lakes, NJ) and placed into an ice bath until the last blood sample was collected.

Blood for Hct analysis was drawn into heparinized microcapillary tubes and centrifuged at 3000 rpm (IEC MicroMB; International Equipment, Co., Needham Heights, MA) for 5 min and read using a microcapillary reader (Model IEC 2201; Damon/IEC, Needham Heights, MA). Hemoglobin concentration ([Hb]) was measured by mixing 20 μL of whole blood with 5 mL of cyanomethemoglobin reagent, and the absorbance was read at 540 nm on a standard spectrophotometer (Smartspec 3000; Bio-Rad, Hercules, CA). Hct and [Hb] were measured in triplicate immediately after sampling and averaged for each blood sample for statistical analysis and calculations. Hct and [Hb] measurements were used to calculate changes in plasma volume (PV) per the Dill and Costill equation (11).

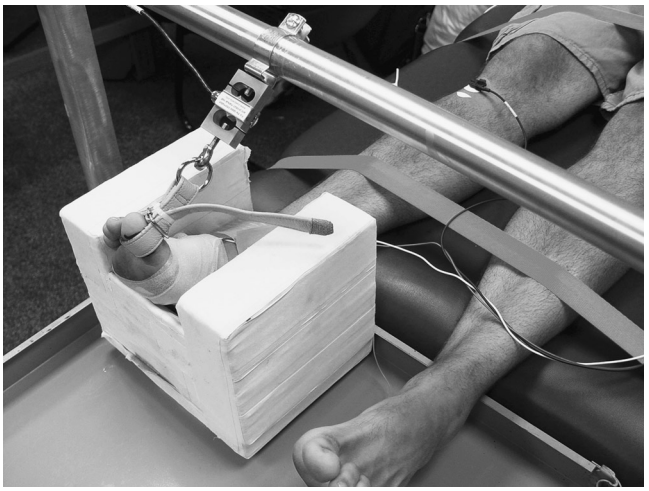

FIGURE 1—Great toe harness and strain gauge attachment.

The remaining 4 mL of blood was centrifuged at 3000 rpm for 15 min at 3°C (Eppendorf Centrifuge 5403; Eppendorf North America, Inc., New York, NY). Plasma was removed from the packed red blood cells, and plasma sodium concentration ($[Na^+]_p$), plasma potassium concentration ($[K^+]_p$), plasma magnesium concentration ($[Mg^{2+}]_p$), and plasma calcium concentration ($[Ca^{2+}]_p$) were analyzed using an ion-selective electrode system (NOVA 8 electrolyte analyzer; Nova Biomedical, Waltham, MA). Plasma osmolality (OSM_p) was determined using freezing point depression osmometry (Model 3D3 Osmometer; Advanced Instruments, Inc., Norwood, MA). Plasma electrolyte concentrations and OSM_p were measured in duplicate and averaged for statistical analyses. An OSM_p of ≥290 mOsm·kg^{-1} H_2O was used to indicate hypohydration (28).

Sweat analysis procedures. Sweat patches were collected after 45 min of exercise. Sweat was separated from the sterile patches via centrifugation and analyzed in duplicate with an ion-selective electrode analyzer for sweat sodium concentration ($Sw_{[Na]}$), sweat potassium concentration ($Sw_{[K]}$), sweat magnesium concentration ($Sw_{[Mg]}$), and sweat calcium concentration ($Sw_{[Ca]}$). Whole-body sweat rate (L·h^{-1}) was calculated by subtracting postexercise body weight from preexercise body weight and dividing by total exercise duration (1 kg of body mass lost represented 1 L of fluid lost). Total sweat electrolytes lost (mmol) were estimated by multiplying electrolyte concentration (mmol·L^{-1}) by total sweat volume (L).

Urine analysis procedures. Urine volume was measured using appropriately sized graduated cylinders. Urine sodium concentration ($U_{[Na]}$), urine potassium concentration ($U_{[K]}$), urine magnesium concentration ($U_{[Mg]}$), and urine calcium concentration ($U_{[Ca]}$) were measured in duplicate using an ion-selective electrode system. Urine electrolyte content (mmol) was calculated by multiplying urine volume (L) at each sampling point by electrolyte concentration (mmol·L^{-1}). Total urinary electrolytes lost were determined by adding the electrolytes lost at each time point.

Fluid analysis procedures. Pickle juice and deionized water were analyzed for $[Na^+]$, $[K^+]$, $[Mg^{2+}]$, $[Ca^{2+}]$, pH, and osmolality in duplicate and averaged for statistical analysis. Electrolytes were analyzed using an ion-selective electrode analyzer. Fluid pH was measured with a pH meter (AR15; Fisher Scientific, Pittsburgh, PA). Osmolality was measured by freezing point depression osmometry.

Statistical analysis procedures. Data are presented as means ± SE. To determine the effects of pickle juice and deionized water ingestion on cramp duration, we used an ANCOVA with MF_{trt} and cramp intensity as covariates. Because the covariates were insignificant, we removed the covariates from the analysis and used a 2 × 2 repeated-measures ANOVA. The cramp duration after the dehydration

protocol (i.e., no fluid ingested) was compared with the cramp duration after ingestion of each drink using repeated-measures ANOVA. Similarly, the intensity of the cramps induced when subjects ingested each fluid and the MF_{trt} was compared with a repeated-measures ANOVA.

Mean plasma, sweat, and urine electrolyte concentrations and contents, osmolality, and volume were analyzed with a 2×3 repeated-measures ANOVA (fluid and time) to assess differences between fluids over time for these variables. Because the fluid $\times$ time interaction was insignificant for all variables but several time effects were significant, we reexamined each fluid trial separately using a one-way ANOVA for repeated measures on time and used the Tukey-Kramer *post hoc* multiple-comparison test to identify which time points were different from baseline. All statistical analyses were performed with Number Cruncher Statistical Software (NCSS 2007, Kaysville, UT). Significance was set at $P \leq 0.05$.

RESULTS

Effects of deionized water and pickle juice ingestion on electrically induced muscle cramps. Subjects self-reported compliance with testing instructions before each experimental day. Cramp duration, intensity, and MF_{trt} data before and after fluid ingestion can be found in Table 1. Cramp duration ($F_{1,9} = 0$, $P = 0.95$), cramp intensity ($F_{1,9} = 0.85$, $P = 0.4$), and MF_{trt} ($F_{1,9} = 1.2$, $P = 0.3$) were similar during the initial cramp induction before each fluid's ingestion. During muscle cramp induction combined with fluid ingestion, cramp intensity was again similar between fluids ($F_{1,9} = 3.1$, $P = 0.11$). Also, compared with before ingestion, cramp intensity was not different after ingestion of pickle juice ($F_{1,9} = 0.1$, $P = 0.79$) and deionized water ($F_{1,9} = 0$, $P = 0.96$).

Cramp duration was 49.1 ± 14.6 s shorter after pickle juice ingestion than after deionized water ingestion ($F_{1,9} = 11.3$, $P = 0.008$). Moreover, cramp duration after ingestion of pickle juice was 68.6 ± 23.2 s shorter than before ingestion ($F_{1,9} = 8.7$, $P = 0.02$). In contrast, ingesting deionized water did not significantly affect cramp duration compared with before ingestion ($F_{1,9} = 4.1$, $P = 0.1$).

Fluid composition. Subjects ingested 73.9 ± 2.7 mL of pickle juice and 73.9 ± 2.8 mL of deionized water. Pickle juice contained a higher $[Na^+]$, $[K^+]$, $[Mg^{2+}]$, and $[Ca^{2+}]$, had a higher osmolality, and had a lower pH than deionized water ($F_{1,1} > 615.9$, $P < 0.02$; Table 2). Total electrolyte content ingested was 72.4 ± 2.6 mmol of Na^+, 0.5 ± 0.02 mmol of K^+, 0.9 ± 0.03 mmol of Mg^{2+}, and 1.7 ± 0.06 mmol of Ca^{2+} with pickle juice and 0 mmol of Na^+, K^+, Mg^{2+}, and Ca^{2+} with deionized water.

TABLE 1. Cramp duration, intensity, and MF_{trt} before (Pre) and after (Post) ingestion of pickle juice and deionized water.

	Pickle Juice		Deionized Water	
	Pre	Post	Pre	Post
Duration (s)	153.2 ± 23.7	84.6 ± 18.5*,**	151.9 ± 12.9	133.7 ± 15.9
Intensity (% of MVIC EMG activity)	68.0 ± 9	66.0 ± 9	60.0 ± 6	55.0 ± 9
MF_{trt} (Hz)	20.4 ± 2.1	—	22.2 ± 1.8	—

Values are means ± SE ($n = 10$).
* Significantly different from after ingestion of deionized water ($P < 0.05$).
** Significantly different from before ingestion ($P < 0.05$).

TABLE 2. Drink composition.

	Pickle Juice*	Deionized Water
OSM (mOsm·kg^{-1} H_2O)	1323.5 ± 0.5	1.0 ± 0
pH	3.15 ± 0.003	6.0 ± 0.09
Specific gravity	1.022 ± 0	1.0 ± 0
$[Na^+]$ (mmol·L^{-1})	978.5 ± 2.5	ND
$[K^+]$ (mmol·L^{-1})	7.0 ± 0	ND
$[Mg^{2+}]$ (mmol·L^{-1})	12.4 ± 0.2	ND
$[Ca^{2+}]$ (mmol·L^{-1})	23.4 ± 0.25	ND

Values are means ± SE ($n = 2$).
* Pickle juice different from deionized water for all dependent variables ($P < 0.05$).
$[Ca^{2+}]$, calcium concentration; $[K^+]$, potassium concentration; $[Mg^{2+}]$, magnesium concentration; $[Na^+]$, sodium concentration; ND, nondetectable; OSM, osmolality.

Blood analysis. Plasma osmolality did not differ between pickle juice and deionized water over time ($F_{2,18} = 0.2$, $P = 0.82$; Table 3). However, OSM_p increased slightly over time; OSM_p increased to 296.4 ± 1.2 mOsm·kg^{-1} H_2O 1 min after pickle juice ingestion ($P < 0.05$) but quickly returned to baseline levels after 5 min (296.2 ± 1.4 mOsm·kg^{-1} H_2O, $P > 0.05$). Similar changes occurred after deionized water ingestion, although OSM_p remained elevated at 5 min after ingestion ($P < 0.05$). The increase in OSM_p after ingestion of each fluid is likely due to a shift of hypotonic fluid out of the intravascular space rather than to an increase in osmoles because of fluid ingestion. This hypothesis was confirmed by the small, but significant, decreases in PV after ingestion over time ($F_{2,18} = 13.15$, $P < 0.001$). However, no differences in PV occurred between pickle juice and deionized water over time ($F_{2,18} = 0.14$, $P > 0.05$), and PV returned to baseline 5 min after ingestion of each fluid ($P > 0.05$; Table 3).

Despite pickle juice having a significantly higher electrolyte content than deionized water, there were no significant differences between fluids after ingestion for $[Na^+]_p$ ($F_{2,18} = 1.26$, $P = 0.31$), $[K^+]_p$ ($F_{2,18} = 0.14$, $P = 0.87$), $[Mg^{2+}]_p$ ($F_{2,18} = 0.39$, $P = 0.68$), or $[Ca^{2+}]_p$ ($F_{2,18} = 0.06$, $P = 0.94$; Table 3). However, deionized water ingestion resulted in a small increase in $[Na^+]_p$ at 1 min after ingestion ($P < 0.05$), which returned to baseline after 5 min ($P > 0.05$). This increase in $[Na^+]_p$ is also likely due to the decrease in PV rather than to an increase in Na^+ content in the intravascular space. Contrastingly, $[K^+]_p$ decreased over time ($F_{1,9} = 15.09$, $P < 0.001$) and was significantly lower at 5 min after ingestion for both pickle juice and deionized water ($P < 0.05$) but was not outside normal clinical values. No changes in $[Mg^{2+}]_p$ or $[Ca^{2+}]_p$ occurred between drinks ($F_{1,9} < 1.11$, $P > 0.32$) or up to 5 min after ingestion of pickle juice or deionized water ($F_{2,18} < 1.98$, $P > 0.17$).

Exercise-induced hypohydration. Subjects lost similar amounts of body weight ($F_{1,9} = 0.38$, $P = 0.55$) and were similarly hypohydrated on each experimental day

TABLE 3. Plasma variables before and after ingestion of pickle juice and deionized water.

	$[Na^+]_p$ (mmol·L^{-1})	$[K^+]_p$ (mmol·L^{-1})	$[Mg^{2+}]_p$ (mmol·L^{-1})	$[Ca^{2+}]_p$ (mmol·L^{-1})	OSM_p (mOsm·kg^{-1} H_2O)	PV (% Δ from Pre)
Pickle juice						
Before ingestion	145.9 ± 0.5	4.37 ± 0.1	0.50 ± 0.01	1.14 ± 0.01	295.4 ± 1.3	—
1 min after ingestion	146.3 ± 0.5	4.41 ± 0.1	0.50 ± 0.01	1.15 ± 0.02	296.4 ± 1.2*	−2.6 ± 0.7*
5 min after ingestion	145.9 ± 0.6	4.29 ± 0.1**	0.51 ± 0.01	1.15 ± 0.01	296.2 ± 1.4	−1.2 ± 0.8
Deionized water						
Before ingestion	145.5 ± 0.4	4.35 ± 0.1	0.50 ± 0.01	1.14 ± 0.01	295.1 ± 0.8	—
1 min after ingestion	146.3 ± 0.4*	4.42 ± 0.1	0.50 ± 0.01	1.15 ± 0.01	296.3 ± 0.9*	−3.0 ± 0.7*
5 min after ingestion	145.9 ± 0.4	4.28 ± 0.1**	0.50 ± 0.01	1.15 ± 0.01	295.8 ± 0.9*	−1.1 ± 0.9

Values are means ± SE (n = 10).
* Significantly different from before ingestion ($P < 0.05$).
**Significantly different from 1 min after ingestion ($P < 0.05$).
$[Ca^{2+}]_p$, plasma calcium concentration; $[K^+]_p$, plasma potassium concentration; $[Mg^{2+}]_p$, plasma magnesium concentration; $[Na^+]_p$, plasma sodium concentration; OSM_p, plasma osmolality.

($F_{1,9} = 0.09$, $P = 0.78$). Thus, data were combined (n = 10). Subjects lost 3.04% ± 0.1% body weight via exercise-induced sweating, which resulted in significant hypohydration after exercise (OSM_p = 295.1 ± 1.1 mOsm·kg^{-1} H_2O).

Sweat volume and electrolyte losses. Subjects lost similar amounts of sweat ($F_{1,9} = 0.1$, $P = 0.76$) and had similar $Sw_{[Na]}$ ($F_{1,9} = 0$, $P = 0.96$), $Sw_{[K]}$ ($F_{1,9} = 0.1$, $P = 0.75$), $Sw_{[Mg]}$ ($F_{1,9} = 0.07$, $P = 0.79$), and $Sw_{[Ca]}$ ($F_{1,9} = 0$, $P = 0.99$) on each experimental day. Therefore, sweat data were combined (n = 10). Subjects had an $Sw_{[Na]}$ of 65.9 ± 4.2 mmol·L^{-1}, $Sw_{[K]}$ of 5.1 ± 0.2 mmol·L^{-1}, $Sw_{[Mg]}$ of 1.5 ± 0.1 mmol·L^{-1}, and $Sw_{[Ca]}$ of 1.4 ± 0.1 mmol·L^{-1}. Subjects lost a total of 2.2 ± 0.1 L of sweat, 144.9 ± 9.8 mmol of Na^+, 11.2 ± 0.4 mmol of K^+, 3.3 ± 0.3 mmol of Mg^{2+}, and 3.1 ± 0.1 mmol of Ca^{2+} as a result of the exercise protocol. The high $Sw_{[Na]}$ indicated that our subjects were unacclimated to exercising in a hot environment (1,7).

Urine volume and electrolyte losses. Because the first and second urine samples were collected before exercise while the subjects were euhydrated, the data from these samples were combined and represent the preexercise condition. Urine sample 3 was collected immediately after the last bout of exercise and therefore represents the urine produced during exercise. Urine samples 4 and 5 were collected 90 and 120 min after exercise. Because these samples were representative of subjects in a hypohydrated state, they were combined for analysis and represent urine produced after exercise.

Subjects had similar urine volumes ($F_{1,9} = 0.7$, $P = 0.43$), urine flow rates ($\dot{U}$, $F_{1,9} = 0.7$, $P = 0.43$), $U_{[Na]}$ ($F_{1,9} = 3.2$, $P = 0.11$), $U_{[K]}$ ($F_{1,9} = 0.05$, $P = 0.84$), $U_{[Mg]}$ ($F_{1,9} = 0.55$, $P = 0.48$), and $U_{[Ca]}$ ($F_{1,9} = 0.47$, $P = 0.51$) on each experimental day over time. There were also no differences between drinks ($F_{1,9} < 3.22$, $P > 0.11$); thus, the urine data were combined (Table 4). However, U_{vol}, $\dot{U}$, $U_{[Na]}$, $U_{[K]}$, and $U_{[Mg]}$ changed over time ($F_{2,18} > 10.6$, $P < 0.001$). Urine volume and $\dot{U}$ were lower after exercise and after ingestion than before exercise ($P < 0.05$). Urine [Na] was higher after ingestion than during and before exercise ($P < 0.05$). Urine [K] increased after exercise as well as after ingestion ($P < 0.05$). Urine [Mg] was only elevated after ingestion compared with baseline ($P < 0.05$), and no changes in $U_{[Ca]}$ occurred during the experiment ($F_{2,18} = 2.3$, $P = 0.12$). Overall, subjects lost a total of 1.0 ± 0.1 L of urine, 45.1 ± 3.7 mmol of Na^+, 23.7 ± 1.4 mmol of K^+, 0.35 ± 0.1 mmol of Mg^{2+}, and 0.47 ± 0.1 mmol of Ca^{2+} via urination.

Total fluid and electrolyte losses. Overall, subjects lost a total fluid volume of 3.2 ± 0.2 L, 190.0 ± 8.1 mmol of Na^+, 34.9 ± 1.6 mmol of K^+, 3.7 ± 0.3 mmol of Mg^{2+}, and 3.6 ± 0.1 mmol of Ca^{2+} on each experimental day.

DISCUSSION

The most significant and novel observation of this study was that ingesting small volumes (73.9 ± 2.7 mL) of pickle juice alleviated electrically induced muscle cramps in mildly hypohydrated (3%) humans. Pickle juice required approximately 85 s to alleviate muscle cramps (cramp duration after ingestion ranged from 12 to 219 s). Although this was much longer than the purported claims of pickle juice's efficacy (38), it still relieved a cramp 45% (85 vs 153 s) faster than when no fluid was consumed. In contrast, ingesting similar volumes of deionized water had no therapeutic effect on cramp duration (cramp duration after ingestion ranged from 71 to 246 s). Discrepancies between anecdotal claims of pickle juice's efficacy and our data may be because of the

TABLE 4. Urine measurements taken before, during, and after exercise.

	U_{vol} (L)	$\dot{U}$ (mL·min^{-1})	$U_{[Na]}$ (mmol·L^{-1})	$U_{[K]}$ (mmol·L^{-1})	$U_{[Mg]}$ (mmol·L^{-1})	$U_{[Ca]}$ (mmol·L^{-1})
Before exercise	0.73 ± 0.09	7.6 ± 1.0	35.6 ± 5.9	13.5 ± 3.1	0.16 ± 0.02	0.28 ± 0.03
Exercise	0.21 ± 0.03*	1.3 ± 0.2*	64.7 ± 5.7	41.0 ± 4.2*	0.68 ± 0.2	1.0 ± 0.5
After exercise	0.05 ± 0.01*	0.5 ± 0.1*	111.0 ± 13.3*†	104.2 ± 11.3*†	1.8 ± 0.4*	1.19 ± 0.2

Values are means ± SE (n = 10). Before exercise is a combination of two urine samples collected at ~30 and 90 min before exercise. Exercise refers to a single urine sample collected immediately after the last bout of exercise. After exercise is a combination of two urine samples collected ~90 and 120 min after exercise. The urine sample collected at 120 min was approximately 10 min after ingestion of each fluid.
* Significantly different from before exercise ($P < 0.05$).
† Significantly different from exercise ($P < 0.05$).
$\dot{U}$, urine flow rate; $U_{[Ca]}$, urine calcium concentration; $U_{[K]}$, urine potassium concentration; $U_{[Mg]}$, urine magnesium concentration; $U_{[Na]}$, urine sodium concentration; U_{vol}, urine volume.

type of cramp alleviated (EAMC vs electrically induced muscle cramps) or errors by these clinicians (38) in their estimation of cramp duration.

The rapidity with which pickle juice relieves electrically induced muscle cramps likely cannot be attributed to spontaneous cramp cessation, weakness of the induced muscle cramps, a placebo effect, or a lack of fluid and electrolyte losses because of our experimental protocol. Cramps induced 30 min before pickle juice ingestion lasted almost twice as long (150 s) as when subjects ingested pickle juice, making it unlikely that the cramps dissipated spontaneously. Moreover, subjects experienced moderately intense cramps on ingestion of pickle juice (66% of MVIC EMG activity) and deionized water (55% of MVIC EMG activity). Although a substantial placebo effect can exist when studying skeletal muscle cramp treatments (24), both the primary investigator and subjects were blinded as much as possible to the fluid being ingested. Subjects had their noses plugged while ingesting the fluids and were not told what they were going to drink or any potential effects of the fluid on the electrically induced muscle cramps. However, subjects were likely able to identify one fluid as pickle juice on tasting it. Regardless, it is unlikely that pickle juice's efficacy can be attributed to a psychological phenomenon. Finally, our subjects lost significant amounts of Na^+, K^+, Mg^{2+}, and Ca^{2+} as a result of the experimental protocol. In fact, our subjects lost similar amounts of fluid and electrolytes as athletes who develop EAMC during athletic competitions (32). Therefore, a lack of electrolyte or body mass losses because of our experimental protocol is an unlikely explanation for the pickle juice's effects on electrically induced muscle cramps.

It is also unlikely that pickle juice's effects on muscle cramp duration are due to the changes in plasma electrolytes or body fluid chemistry, as believed by 64% (226/353) of athletic trainers who provide pickle juice to their cramping athletes (22). Three reasons refute this hypothesis. First, the amount of electrolytes ingested with 1 $mL \cdot kg^{-1}$ body weight of pickle juice has a negligible effect on extracellular fluid electrolyte concentrations (<1.5 $mmol \cdot L^{-1}$) (23). Previous work in our laboratory has demonstrated that no changes in $[Na^+]_p$, $[K^+]_p$, $[Mg^{2+}]_p$, $[Ca^{2+}]_p$, PV, or OSM_p occur after ingestion of 1 $mL \cdot kg^{-1}$ body weight of pickle juice or water in euhydrated rested humans (23). The results of the present study not only confirm these observations but also extend them to include hypohydrated individuals. Second, 85 s is not enough time for the nutrients in pickle juice to be emptied from the stomach, absorbed by the small intestines, and assimilated into the extracellular fluid compartment. Small volumes of pickle juice (150 mL) require approximately 30 min to leave the stomach in rested euhydrated humans (unpublished observations). The slow gastric emptying is likely due to the high osmolality, low pH, and small volume of the pickle juice ingested. Moreover, hypohydration would, theoretically, further impair gastric emptying (27), making it even more unlikely that the electrolytes in pickle juice were absorbed quickly enough to cause cessation of the electrically induced muscle cramp. Third, even if all the electrolytes present in pickle juice were immediately absorbed and circulated to the cramping muscle, subjects would still have substantial electrolyte and fluid losses. On the basis of the volume of pickle juice ingested, its electrolyte content, and the volume and electrolytes lost during experimentation, pickle juice would only restore 2% (0.074/3.2 L) of fluid, 38% (72.4/190.0 mmol) of Na^+, 1% (0.5/34.9 mmol) of K^+, 24% (0.9/3.7 mmol) of Mg^{2+}, and 47% (1.7/3.6 mmol) of Ca^{2+}.

Considering these points, we speculate that pickle juice ingestion triggers a reflex, likely somewhere in the oropharyngeal region, which acts to reduce alpha motor neuron pool activity in cramping muscles. Oropharyngeal stimulation is known to elicit simple and complex reflexes that involve the modulation of alpha motor output in the cephalic region (e.g., glossopharyngeal–hypoglossal reflex), upper gastrointestinal tract, and airway (2,19). Chemical stimulation by acetic acid (a primary ingredient in pickle juice) is effective at eliciting these oropharyngeal reflexes (13). Because acetic acid has been shown to elicit reflexive motor responses in the oropharyngeal region, it may not be outside the realm of possibility that its ingestion triggers an inhibitory motor reflex to skeletal muscles undergoing cramp.

We propose two scenarios by which pickle juice ingestion may cause inhibition of a cramping muscle's alpha motor neuron pool. First, pickle juice may trigger an inhibitory stimulus from a supraspinal source that activates inhibitory interneurons. Activation of these interneurons may postsynaptically inhibit the alpha motor neuron pool of the cramping muscle. In rats, intraperitoneal injection of acetic acid increases the release of inhibitory neurotransmitters (e.g., serine and glycine) in the dorsal horn of the spinal cord (12). Glycine is a specially potent inhibitory neurotransmitter in the spinal cord that may increase inhibitory interneuron activity (e.g., Renshaw cells) or decrease ventral horn neuron activity (9) because these neurons have a high affinity for glycine (37). Suppression of inhibitory neurotransmitters has been implicated as a possible mechanism for cramp genesis (26). Thus, an increase in inhibitory neurotransmitter activity, triggered by pickle juice ingestion, could be involved in the alleviation of electrically induced muscle cramps.

Second, this inhibitory supraspinal signal may override stimuli of an excitatory nature coming from a small group of muscle afferent fibers that were activated by the percutaneous electrical stimulation, muscle contraction/cramp, or both. Although the cramp induction model we used is generally well tolerated (20,34), some pain and, thus, small-diameter muscle afferent (e.g., Types III and IV) stimulation undoubtedly occurred. Activation of these small group muscle afferents can affect cramp generation or sustainability (31). Serrao et al. (31) observed that injection of hypertonic saline into the FHB-induced muscle pain and facilitated the generation of muscle cramp. They concluded that enhanced activation of these small-diameter muscle afferents resulted in an increased susceptibility to cramp.

Because we did not apply a proximal nerve block to the tibial nerve, we cannot rule out the possibility that small-diameter muscle afferent activation occurred and helped maintain the cramp.

Regardless of where the inhibition is occurring, pickle juice's apparent reduction of alpha motor neuron activity is consistent with current thought on the etiology of EAMC. Schwellnus et al. (29) proposed that EAMC were due to neuromuscular fatigue. Neuromuscular fatigue is thought to create an imbalance between muscle spindle and Golgi tendon organ activity, resulting in increased alpha motor neuron excitability. Thus, if EAMC are caused by an imbalance between excitatory and inhibitory stimuli at the alpha motor neuron pool, pickle juice ingestion may cause an increase in inhibition from supraspinal sources, thereby resulting in cramp alleviation.

It is unknown which ingredient in pickle juice may initiate this inhibitory reflex. We propose that it is the acetic acid (vinegar) in pickle juice, not the electrolyte content, which triggers this reflex. Acetic acid has been shown to cause motor reflexes in the muscles of the larynx and pharynx (13). Moreover, there is anecdotal support for acetic acid ingestion also relieving EAMC. Williams and Conway (39) observed in one subject that when vinegar was ingested instead of pickle juice, less vinegar was required to alleviate the EAMC and the EAMC was alleviated faster. Therefore, anecdotally, acetic acid seems capable of alleviating EAMC irrespective of the Na^+ content of the drink. These claims remain to be verified scientifically, however, and must be used cautiously because they only occurred in one subject.

In conclusion, pickle juice, and not deionized water, significantly shortens electrically induced muscle cramp duration in mildly hypohydrated humans. How pickle juice decreases cramp duration is unknown; however, we hypothesize that it triggers an inhibitory oropharyngeal reflex shortly after ingestion, which reduces alpha motor neuron activity to cramping muscles. The decrease in cramp duration after pickle juice ingestion is likely not due to the changes in body fluid chemistry, a placebo effect, spontaneous cessation, or a lack of fluid and electrolyte loss because of experimentation. The ingredient in pickle juice that elicits the decrease in cramp duration is also unknown, although acetic acid could play a role in triggering an oropharyngeal reflex.

The results of the present study do not constitute endorsement by the American College of Sports Medicine.

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