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# The Effects of Hypohydration on Neurocognitive, Balance, Vestibular Ocular Motor Functions and Mood State

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The Effects of Hypohydration on Neurocognitive, Balance, Vestibular Ocular Motor Functions and Mood State

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**Abstract**

**Introduction:** Inconsistent findings have been observed on the impact of hydration state on cognitive functions. The isolated effect of hypohydration on neurocognitive performance, balance, vestibular ocular motor function and mood outcomes in widely used concussion assessment tools has not been studied. The purpose of this study was to investigate how hypohydration affected the results in concussion testing batteries. **Methods:** A single-blind randomized crossover design was used. Thirteen healthy males (22 ± 4y, 180.9 ± 5.7cm) without history of concussion within the past six months or any condition or disease that could influence outcome measurements participated in this study. Each subject completed concussion tests in two different conditions, hypohydrated (HYP) and euhydrated (EU) trials. During HYP, subjects restricted fluid and fluid-rich foods for 20 hours prior to the testing. Testers who were blinded to a trial assignment performed the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT), Sport Concussion Assessment Tool 3 (SCAT3), King Devick (K-D), and a brief vestibular ocular motor screening (VOMS) in a randomized order. Following testing, NASA Load Index and Effort Questionnaire were assessed. **Results:** No significant differences were observed on ImPACT, Sideline Assessment for Concussion (SAC), Balance Error Scoring System (BESS) and the Tandem Walk in SCAT3, K-D, symptom provocation in VOMS and NASA Load Index and Effort Questionnaire ($p > .05$). HYP increased number ($p = .026$) and severity of symptoms ($p = .020$) assessed in SCAT3 compared with EU. Additionally, subjects reported higher symptoms in VOMS during HYP ($p < .05$). **Conclusion:** Hypohydration produced concussion related symptoms. Our findings suggested that hypohydration did not negatively influence neurocognitive, balance, or vestibular ocular motor performance in the common concussion assessment testing tools.

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## Table of Contents

# Chapter 1: Introduction

Concussion is a brain injury that occurs due to biomechanical forces and affects brain function (causes alteration in mental status).[1] Concussion is one of the biggest concerns in the field of sports medicine. Concussions have been reported in a wide variety of sports and in both genders.[2] Concussion commonly occurs in sports regardless of type, level of participation or gender. Recently, the potential long-term consequences of sport-related concussion has raised awareness and garnered media attention. This increased attention has vastly expanded the amount of research related to concussion. Concussion is known to cause numerous symptoms including but not limited to headache, dizziness, nausea, and difficulty concentrating.[1, 3] Because of various symptoms, current recommendations involve implementing multiple tests including symptom checklists, motor control tests, mental status and neurocognitive tests when screening for and evaluating concussion.[1, 3] These evaluative tests are designed to investigate each component related to concussion. It is recommended that Clinicians should integrate the information obtained from each test to evaluate concussion. Thus, concussion is difficult to screen for and manage appropriately.

One of the reasons why it is complicated to provide proper evaluation and management of concussion is that other health issues mimic the symptoms and signs of concussion. Broglio et al. (2007) stated that sleep deprivation, fatigue or stimulant use could complicate concussion management.[4] Some studies have investigated the influence of sleep deprivation on brain function and report that sleep deprivation could impair neurocognitive function such as reaction time, verbal memory and visual memory.[5-7]

Poor hydration status can also mimic concussion and compromise accurate diagnosis. Hypohydration is the physiological state in which the body does not possess enough water to maintain proper functions. Hypohydration is a common consequence of athletic participation.[8] Hypohydration related symptoms include headache, dizziness, nausea, vomiting and fatigue.[9, 10] These are identical to the symptoms produced by concussion.[1, 3] Therefore, it is speculated that hypohydration could affect symptom reporting and performance on concussion assessment tests, and complicate management of sports-related concussion. To the best of our knowledge, there is only one research study that investigated the influence of fluid loss on outcomes of concussion test batteries at this point. Patel et al. (2007) reported that hypohydration increased concussion related symptom severity and number, and impaired visual memory.[11] However, this research included exercise fatigue as a potential confounding factor and used a limited test battery for outcomes. Furthermore, previous research studying the influence of hydration state on cognitive function and mood did not establish body mass baselines in a hydrated state. The isolated effect of hypohydration on concussion-related outcomes has yet to be verified. Improvement of diagnostic accuracy for concussion is essential to establish proper management and prevention of concussion. Therefore, additional research investigating the effect of hypohydration on recommended concussion assessments is warranted.

The purpose of this research was to investigate the influence of mild hypohydration on a battery of recommended concussion assessment methods. It was hypothesized that mild hypohydration would negatively affect neurocognitive performance, postural balance, vestibular ocular motor function and mood state. As concussion is prevalent in sports and mild hypohydration commonly occurs among athletes, these findings could potentially improve sport-related baseline assessment and subsequent management.

# Chapter 2: Literature Review

## Effects of Hypohydration on Mood

Mood is a mental state that is subjective to a change in environment. The negative influence of hypohydration on mood state has been consistently reported. Hypohydrated participants reported mental states such as tiredness, less concentration, tension, confusion and depression.[11-23] These studies showed that water deprivation could affect self-reported mood. It has been shown that mood is sensitive to hydration status. However, the negative influence of hypohydration on mood is observed in limited components of mood.[11-23]

## Effects of Hypohydration on Neurocognitive Function

The influence of hypohydration on neurocognitive performance has been under debate. (Table 1) Some experiments demonstrated the negative effect on neurocognitive function.[11, 13-17, 19, 20, 24-28] In contrast, other studies reported no neurocognitive deficit with hypohydration.[12, 18, 23, 29, 30] One of the potential factors for these incongruent outcomes is the dehydrating methodology variation in many studies.

Table 1. Characteristics of Research Investigating the Influence of Hypohydration on Mood and/or Neurocognitive Function

| Authors | Interventions | Hydration measurements | Outcomes (Mood) | Outcomes (Neurocognitive function) |
|---|---|---|---|---|
| Patel et al. (2009) | Exercise & fluid restriction | USG, BM | Increased headache, feeling slowed down | Decreased visual memory |
| | | | Difficulty concentrating, increased fatigue | |
| Ackland et al. (2008) | Bowel preperation | Bioelectrical impedance, BM | Increased anxiety | No impairment |
| Armstrong et al. (2012) | Trial 1: Exercise | USG, BM | Increased anger, headache | Increased false alarms in visual vigilance |
| | Trial 2: Exercise & diuretic | | Increased fatigue and task difficulty | |
| | Trial 3: Exercise & fluid replacement | | Decreased vigor and concentration | |
| Baker et al. (2007) | Trial 1: Exercise & carbohydrate drink | BM | Increased lightheaded | Slower reaction time |
| | Trial 2: Exercise & fluid | | Increased hotness | Increased errors in attentional performance |
| | Trial 3-6: 1-4% hypohydration | | Increased fatigue | |
| Cian et al. (2001) | Trial 1: Heat exposure & fluid restriction | BM | Increased fatigue | Slower reaction time |
| | Trial 2: Heat exposure & fluid replacement | | | Decreased short-term memory |
| | Trial 3: Exercise | | | |
| | Trial 4: Control | | | |
| Cian et al. (2000) | Trial 1: Hyperhydration | BM | Increased fatigue | Increased tracking error |
| | Trial 2: Heat exposure | | | Slower reaction time |
| | Trial 3: Exercise | | | Decreased short-term memory |
| | Trial 4: Control | | | |
| D'anci et al. (2009) | Exercise & fluid restriction | BM | Increased fatigue, anger, depression | Increased short-term memory |
| | | | Increased tension and confusion | Decreased vigilance |
| | | | Decreased vigor | |
| Ely et al. (2013) | Exercise, heat exposure & fluid restriction | USG, BM | Increased anger, depression and fatigue | No impairment |
| Ganio et al. (2011) | Trial 1: Exercise | USG, BM | Increased anxiety | Slower reaction time |
| | Trial 2: Exercise & diuretic | | Increased fatigue | Increased false alarms in visual vigilance |
| | Trial 3: Exercise & fluid replacement | | | |
| Petri et al. (2006) | Fluid restriction | None | Less energy | Increased task solving time |
| Pross et al. (2013) | Fluid restriction | USG, Ucol, Uvol | Increased fatigue and confusion | N/A |
| Shirreffs et al. (2004) | Fluid restriction | Uosm, Uvol, BM | Increased headache, fatigue | N/A |
| | | | Decreased concentration | |
| Szinnaci et al. (2005) | Fluid restriction | Uosm, BM | Increased fatigue | No impairment |
| | | | Decreased alertness | |
| Ainslie et al. (2002) | Exercise | Uosm, BM | N/A | Slower reaction time |
| Bar-David et al. (2005) | Natural hydration status | Uosm | N/A | Decreased short-term memory |
| Gopinathan et al. (1988) | Heat exposure, exercise & fluid restriction | BM | N/A | Decreased short-term memory |
| | | | | Decreased arithmetic efficiency |
| | | | | Decreased visuomotor function |
| Lindseth et al. (2013) | Low-fluid diet | BM | N/A | Decreased working memory |
| Sharma et al. (1986) | Heat exposure, exercise & fluid restriction | BM | N/A | Decreased working memory |
| | | | | Decreased psychomotor performance |
| Adam et al. (2008) | Trial1: Exercise | BM | N/A | No impairment |
| | Trial2: Exercise, fluid restriction & cold stress | | | |
| | Trial3: Heat exposure | | | |
| | Trial4: Exercise, fluid restriction & temperate environment | | | |
| Kempton et al. (2011) | Exercise | Uosm, BM | No change | No impairment |

USG: Urine specific gravity, BM: Body mass, Ucol: Urine color, Uvol: Urine volume, Uosm: Urine osmolality

**-Exercise Stress-**

Several studies used exercise to induce hypohydration. Ainslie et al. (2002) drove subjects to a hypohydrated state by exercise stress.[24] They reported that hypohydrated subjects demonstrated psychomotor function impairment. Similarly, some authors showed that subjects with exercise-induced hypohydration indicated reductions in neurocognitive functions.[13, 15, 16] In contrast, another study did not reveal neurocognitive deficit among subjects who were hypohydrated after completing exercise.[30] The intensity, duration and types of exercis used in these studies were different. These heterogeneous interventions could cause varied outcomes. Exercise itself has been shown to enhance neurocognitive function.[31-33] On the other hand, studies demonstrate that fatigue can impair cognitive performance.[34-36] Applying exercise stress prior to neurocognitive tests could modify outcomes and would make it difficult to investigate the isolated influence of hypohydration.

**-Heat Exposure-**

Heat stress was used as a dehydrating method in several research studies. Cian et al. (2000) found that reaction time and memory function were impaired after heat-induced hypohydration.[16] Similarly, another study reported that hypohydrated subjects who were exposed to heat stress demonstrated decreased neurocognitive functions such as vigilance, processing speed and psychomotor ability.[15] On the other hand, no neurocognitive impairment was observed in the previous study that utilized heat exposure to facilitate dehydration.[29] All of these studies induce hypohydration by exposing subjects to heat stress, but the interventions were not identical. Different methodologies could modify outcomes. Additionally, the subjects with high core temperature demonstrated neurocognitive impairments such as decreased reaction time and visual processing.[37] Core temperature elevation could be a confounding factor. Therefore, it seems inappropriate to expose participants to a high temperature environment prior to investigating the influence of hypohydration on neurocognitive functions.

**-Fluid Restriction-**

Fluid restriction is also a common method to induce hypohydration. Subjects have been asked to refrain fluid and fluid-rich food consumption for a certain period of time to become hypohydrated.[20-23, 27] As with the research cited above, the influences of hypohydration induced by fluid restriction on neurocognitive functions also vary from study to study. Some authors reported the decrease in neurocognitive functions such as processing speed,[20, 27] but the others found no influence.[23] The duration of fluid restriction varies from 15 hours to 37 hours. This could affect the severity of hypohydration and modify neurocognitive functioning.

**-Other Interventions-**

Most researchers employ multiple interventions in combination including exercise tasks, heat exposure, diuretics and fluid restriction.[11, 13-15, 17-19, 26, 28, 29] The various outcomes reported and the influence of hypohydration on neurocognitive performance has remained controversial due to the confounding factors of each intervention.

In addition to exercise, heat and fluid restriction, bowel preparation, which is a pre-surgical cleansing of intestines, was utilized to induce hypohydration. Ackland et al. (2008) found no difference in neurocognitive performance between subjects who received bowel preparation and the subjects who did not.[12] Bar-Davidet al. (2005) did not employ any dehydrating intervention.[25] They compared the neurocognitive function of the subjects who were naturally hypohydrated and the subjects who were naturally euhydrated, and identified memory impairment among hypohydrated subjects.[25]

These different dehydrating methodologies could have varied the outcomes of previous research. It is difficult to conclude that hypohydration affects neurocognitive function because of the diversity in the ways producing hypohydration state.

## Concussion Assessment Test Batteries

### -SCAT3-

Sport Concussion Assessment Tool 2 (SCAT2) was revised and updated at the 4th International Conference on Concussion in Sport in 2012 and Sport Concussion Assessment Tool 3 (SCAT3) was released as a standardized tool for concussion assessment. There is no available study that shows the reliability of SCAT 3 since SCAT3 is new concussion assessment tool. However, SCAT3 contains same component of SCAT2. The components of the SCAT2 have demonstrated acceptable reliability. [38-41] Therefore, it is assumed that SCAT3 is a reliable assessment test.

### -ImPACT-

Neurocognitive assessment is recommended as a part of concussion assessment.[2, 3] Computerized cognitive test battery has been widely adopted because of its ease of administration. Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) was designed as an aid in assessing sports-related concussion among high school, college and professional athletes. ImPACT is one of the most widely used computerized neurocognitive assessment tests. Some investigates have demonstrated acceptable high Intraclass Correlation Coefficient (ICC) vales for the ImPACT composite score ranging from 0.46 to 0.88.[42-45] On the other hand, Broglio et al. (2007) reported low ICC values for each component of the ImPACT 45 days and 50 days after baseline.[46] They found respective ICCs as follows: verbal memory composite (0.23 and 0.40), visual memory composite (0.32 and 0.39), visual-motor speed (0.38 and 0.61) and reaction time composite (0.39 and 0.51). Nakayama et al. (2014) hypothesized that their methodological problems due to providing three computerized cognitive tests in a row could cause these low values, and reexamined their study. They reported high ICCs ranging from 0.60 to 0.91 for the ImPACT composite scores.[47] Based on the current available evidence, the ImPACT is considered as a reliable computerized neurocognitive test.

**-King-Devick Test-**

The King-Devick test (K-D test) was designed for the assessment of saccade. The impairment of eye movement is reported as one of the indicators of suboptimal brain function.[48] Therefore, K-D test has recently been a topic of interest in concussion management because of its use of use and time-efficient to administer. Currently there is only one study that shows the test-retest reliability. Galetta et al. (2011) reported a high degree of test-retest reliability ($ICC > 0.90$).[49] However, the ICC values that they reported were based on the measurements within 15 minutes and the measurements of pre and post boxing match. The test-retest reliability for K-D test within 15 minutes may be clinically limited since it is not realistic to retest K-D test in a short time of period. Also comparing the data obtained prefight and postfight could modify the test outcomes due to multiple confounding factors such as exercise, fatigue and change in core temperature. This research method is not ideal to identify the test-retest reliability. Thus, the test-retest reliability for K-D test is limited at this point.

**-Vestibular Ocular Motor Screen (VOMS) -**

Vestibular Ocular Motor Screen (VOMS) was created for the assessment of vestibular ocular motor impairment through provoking self-reported symptom after each test. Vestibular and ocular motor impairments are common among the patients with concussion.[50,51] VOMS has been used for the part of concussion assessment. However, the test-retest reliability for VOMS has not been identified in scientific research.

## Hydration Status Assessments

Several biomarkers are currently used for hydration assessment. The commonly used measurements are bioelectrical impedance spectroscopy, body mass change, plasma osmolality, plasma volume change, urine osmolality, urine specific gravity (USG), urine conductivity, urine color, urine volume, and saliva osmolality.[52] Measuring plasma osmolality, and total body water via stable isotope dilution or neutron activation analysis is a gold standard for human static hydration status.[53] However, Armstrong (2007) suggested that it is difficult to measure total body water through the day because the amount of body fluid continuously changes during daily activities.[52]

Other biomarkers can be alternative measurement for dynamic hydration status. Urine color is the simplest urinalysis to identify hydration status by comparing the color of urine with color chart. Although urine color is a subjective measurement, it has been shown that urine color assessment is an accurate hydration assessment[54] and has high sensitivity and specificity.[55] Urine osmolality measures total urine solute content via osmometer. Urine osmolality is more variable than other measurements, but values greater than 700 mOsmol/kg indicate hypohydration.[56] It is shown that urine specific gravity and body mass change provide valid assessment of human hydration status.[52] Dynamic hydration is accurately accomplished by measuring urine specific gravity and body mass change. Baker et al. (2009) reported that body mass change measurement is able to assess total body water accurately and reliably.[57] Three consecutive days body mass measurement establish valid baseline body mass.[58] More than 1 % of body weight reduction from baseline is considered as hypohydration.[56] USG is used to identify hydration status by comparing the density of urine with that of pure water. USG can be measured relatively quickly with a refractometer. The value of USG greater than 1.020 indicative of hypohydration.[56]

# Chapter 3: Methods

## Subjects

Thirteen males (age: 22 ± 4y, height: 180.9 ± 5.7cm) voluntarily participated in this study. Every subject attended a briefing and was asked to fill out a medical history form prior to participating in the study. Subjects who had history of physician diagnosed concussion within the past six months, severe cervical spine injury, neurocognitive disorder, migraines, vestibular dysfunction, learning disability or current lower extremity injury that could affect their performance on balance test was excluded from participating in this study. Participants took no medications or substances known to affect neurocognitive function or hydration status. Participants identified English as their primary language. All participants read and signed an informed consent form approved by the University of Arkansas Institutional Review Board.

## Study Design

A single-blind randomized crossover design was used. Participants were randomly assigned to a trial order, but were not blinded. Any concussion battery tester was not aware of hydration status during baseline testing of participants.

## Procedures

Participants were randomly scheduled for two separate trials, either hypohydrated (~2.0% body mass loss) or euhydrated. Participants completed a three-day baseline body weight measurement. They were asked to provide a small urine sample in a urine specimen cup. Researchers recorded participants' nude body mass, USG, urine osmolality and urine color on three consecutive days preceding testing for both trials. USG was analyzed via a hand-held refractometer (Atago, Tokyo, Japan). Urine osmolality was measured in duplicate using a freezing-point depression osmometer (Advanced Instruments, Norwood, Massachusetts). Urine color was determined by comparing the color of urine in a test tube with color chart (www.hydrationcheck.com). Researchers who recorded hydration status and body mass measures were not involved in concussion assessments. Participants were encouraged to drink an extra 500ml of water prior to going to bed and in the morning to maintain euhydration for baseline and euhydrated trial days. For 24 hours prior to each trial, dietary intake was recorded on a standard diet log and analyzed for macronutrient and calorie intake using Nutritionist Pro (Axxya Systems, Stafford, Texas). Exercise was avoided for 15 hours preceding testing. Participants were asked to have at least seven hours sleep the night before trials. They were also advised to refrain from caffeine for 12 hours, and alcohol and tobacco products during the four-day testing protocol. Compliance was verified via self-report upon questioning. Prior to testing, urinalysis and body mass were assessed and any participant with a hydration status that did not meet assigned group requirements was disqualified, and testing was rescheduled. Participants completed their second trial at least two weeks following their initial trial to avoid practice effects.

*Euhydrated trial*: Participants were encouraged to drink an extra 500ml of water prior to going to bed and in the morning to maintain euhydration. Participants completed a 30-45 minute identical aerobic task 15 hours prior to testing for both trials.

*Hypohydrated Trial:* Participants in the hypohydrated trial were instructed not to consume fluids/fluid-rich foods for 20 hours prior to testing and asked to eat similar foods for 24 hours before testing compared to their other trial. Participants completed the same aerobic task as the one provided in euhydrated trial 15 hours prior to the testing to accentuate fluid losses.

**Data Collection**

Participants took a computerized neurocognitive assessment (The Immediate Post-Concussion Assessment and Cognitive Testing: ImPACT), Sport Concussion Assessment Tool (SCAT-3), King Devick test (K-D test), and a brief vestibular ocular motor screening (VOMS) measure in a randomized order. A trained researcher, blinded to group allocation, administered all assessments. All testing was provided at the same time of day for each subject in a thermoneutral environment in order to eliminate the influence of circadian rhythm and room temperature on testing outcomes.

**Concussion Assessment Test Batteries**

**-SCAT3-**

The Sport Concussion Assessment Tool-3 (SCAT-3): The SCAT-3 is comprised of a 22-item graded symptom scale (22 points); a 2-item sign score determining loss of consciousness and balance difficulties (2 points); the Glasgow Coma Scale (GCS) evaluating eye response, verbal response, and motor response (15 points); the Sideline Assessment for Concussion (SAC) for orientation, immediate memory, concentration, and delayed recall (30 points); the modified BESS (30 points); a coordination examination (1 point); and Maddocks questions for sideline assessment. Balance Error Scoring System (BESS). The BESS is a clinical balance test consisting of six test conditions involving three stances performed on both firm and foam surfaces: 1) feet- together, (2) single-leg, and (3) tandem stance. Each condition is performed with the hands placed on the hips for 20 sec. Total errors- including lifting hands off hip, opening eyes (in eyes closed conditions) leaning >30 degrees of flexion/extension or abduction/adduction, stepping out of position, and protracted time out of position- are recorded by trained observers. The total errors across all conditions provide a total BESS error score.

**-ImPACT-**

The Immediate Post Assessment Cognitive Test (ImPACT) and Post Concussion Symptom Scale: Neurocognitive performance and concussion symptoms were assessed using the ImPACT computerized neurocognitive test battery. The ImPACT test was completed individually in a private exam room. The ImPACT neurocognitive test battery comprises three sections. 1) questions about the participant's gender, age, headache, and concussion history; 2) current concussion symptoms including headache, memory problems, confusion, and fogginess; and 3) computers tests of, memory, reaction time, and learning. In the first section, subjects self-report demographic and descriptive information on a series of instructional screens. The demographics include: age, gender, and self-reported history of migraine headaches and previous concussions. In the second section, subjects rate on a 7-point Likert scale the presence of each of 22 common concussion-related symptoms including headache, memory problems, confusion, and fogginess. The third section of the

ImPACT consists of six neurocognitive test modules that evaluate subjects' attention processes, verbal recognition memory, visual working memory, visual processing speed, reaction time, numerical sequencing ability, and learning. This section of the test includes five parallel forms to minimize and control for practice effects.

**-King-Devick Test-**

The King–Devick (K–D) test: The K-D test is based on the time to perform rapid number naming. The test involves reading aloud a series of single digit numbers from left to right on three test cards. Standardized instructions are used. The K–D test includes one demonstration card and three test cards. Subjects are asked to read the numbers on each card from left to right as quickly as possible but without making any errors. The sum of the three test card time scores constitutes the summary score for the entire test. Numbers of errors made in reading the test cards are also recorded.

**-Vestibular Ocular Motor Screen-**

The UPMC Vestibular Ocular Motor Screen (VOMS): The VOMS was developed to assess vestibular and ocular motor impairment via patient-reported symptom provocation following each assessment. The VOMS consists of brief assessments in the following five domains: 1) smooth pursuits, 2) horizontal and vertical saccades, 3) convergence, 4) horizontal and vertical vestibular ocular reflex (VOR) and 5) visual motion sensitivity (VMS). Patients verbally rate changes in headache, dizziness, nausea and fogginess symptoms compared to their pre-assessment state on a scale of 0 (none) to 10 (severe) following each VOMS assessment to determine if each assessment provokes symptoms. Convergence is assessed by both symptom report and measurement of the near point of convergence (NPC). NPC values are averaged across 3 trials. NPC values up to 5 cm are considered normal.

**Effort Assessment**

**-NASA Task Load Index-**

NASA Task Load Index was designed to measure self-perceived workload. Subject rates each mental demand, temporal demand, performance, frustration level and effort using a visual analogue scale after completing given tasks.

**-Effort Questionnaire-**

Effort questionnaire simply asks participants how much effort they put in on a scale of 1 to 4 with 1 being “no effort” and 4 being “high effort”.

**Analysis**

Data were analyzed using SPSS Statistics (version 23.0; IBM SPSS Software, Armonk, New York). Results from hydration assessments, the standard diet log, SCAT3, ImPACT, K-D test, VOMS, NASA Load Task Index, and Effort Questionnaire were compared using a paired samples *t* test. A significance level of $p < .05$ was set priori.

## Chapter 4: Results

*Body Mass and Urinalysis:* All subjects completed baseline body mass and urinalysis assessments in a euhydrated state for three consecutive days prior to each trial. Upon arrival for a euhydration trial, body mass was within one percent of the three-day average, USG was below 1.020, Uosm was under 700 mmol/kg, and Ucol was lighter than 4. Body mass loss from three-day baseline, USG, Uosm and Ucol during the hypohydration protocol day were more than one percent with USG greater than 1.020, Uosm greater than 700mmol/kg and Ucol equal to or darker than 4 respectively. Significant differences were observed in body mass, USG, Uosm, Ucol and body mass reduction between the euhydrated and hypohydrated trials ($p < .001$) (Table 2).

Table 2. Hydration Assessment Outcomes

| | EU Three-day Baseline Ave. | EU | HYP Three-day Baseline Ave. | HYP | *P* value |
|---|---|---|---|---|---|
| BM (kg) | 79.1 ± 10.2 | 79.3 ± 10.2 | 79.0 ± 9.9 | 77.4 ± 10.1 | < .001* |
| USG (U) | 1.010 ± .004 | 1.010 ± .005 | 1.012 ± .007 | 1.024 ± .002 | < .001* |
| Uosm (mmol/kg) | 382 ± 163 | 402 ± 199 | 476 ± 251 | 948 ± 93 | < .001* |
| Ucol | 2 ± 1 | 2 ± 1 | 2 ± 1 | 4 ± 1 | < .001* |
| BM Loss (%) | | .31 ± .58 | | -2.13 ± 1.07 | < .001* |

Values are means ± SD. *P* values reported are the result of paried *t* tests comparing EU with HYP. EU, Euhydration protocol HYP, Hypohydration protocol; BM, Body Mass; USG, Urine Specific Gravity; Uosm, Urine Osmolality; Ucol, Urine Color
*Significant difference between EU and HYP

*Macronutrients and Calorie Intake:* No significant difference was revealed in macronutrients and total calorie intake between the hypohydrated and euhydrated trials.

*SCAT3:* There were significant differences on total number of symptoms and severity between trials (Table 3). The hypohydrated trial significantly increased the severity of symptoms ($p = .020$) and produced a higher number of symptoms ($p = .026$). No significant difference was observed in SAC, BESS or Tandem walk subcomponents of the SCAT3.

Table 3. SCAT3 Scores

| | EU | HYP | *P* value |
|---|---|---|---|
| Total Number of Symptoms | 2.46 ± 3.05 | 6.69 ± 5.44 | .026* |
| Total Symptom Severity | 3.08 ± 3.62 | 12.54 ± 12.18 | .020* |
| SAC | | | |
| Orientation | 5.00 ± .00 | 5.00 ± .00 | - |
| Immediate Memory | 14.69 ± .48 | 14.54 ± .78 | .549 |
| Concentration | 4.08 ± 1.32 | 4.46 ± 1.13 | .096† |
| Delayed Recall | 4.23 ± 1.17 | 4.00 ± 1.23 | .534 |
| BESS (Hard Surface) | | | |
| Double Leg | .00 ± .00 | .00 ± .00 | - |
| Single Leg | 2.15 ± 2.23 | 2.38 ± 2.10 | .774 |
| Tandem | .62 ± 1.12 | 1.00 ± 1.16 | .406 |
| Total Error | 2.77 ± 2.77 | 3.38 ± 2.99 | .570 |
| BESS (Airex) | | | |
| Double Leg | .00 ± .00 | .00 ± .00 | - |
| Single Leg | 5.00 ± 4.12 | 6.31 ± 3.45 | .176 |
| Tandem | 3.85 ± 1.73 | 4.08 ± 2.50 | .774 |
| Total Error | 8.85 ± 3.67 | 10.38 ± 4.25 | .156 |
| Tandem Walk (sec) | 11.28 ± 2.55 | 11.37 ± 2.31 | .856 |

Values are means ± SD. EU, Euhydration protocol; HYP, Hypohydration protocol
SAC, Sideline Assessment for Concussion; BESS, Balance Error Scoring System
*Significant difference between EU and HYP
† Statistical trend toward significance

*ImPACT:* Regardless of hydration state, no significant differences were observed on the ImPACT test, although there were trends that both total number of symptoms ($p$ = .053) and severity ($p$ = .089) were elevated in the hypohydrated trial (Table 4).

Table 4. ImPACT Scores

| | EU | HYP | *P* value |
|---|---|---|---|
| Verbal Memory | 90.42 ± 11.94 | 90.25 ± 9.70 | .955 |
| Visual Memory | 82.00 ± 12.32 | 82.58 ± 14.16 | .782 |
| Visual Motor | 45.35 ± 7.16 | 44.07 ± 6.38 | .307 |
| Reaction Time | .60 ± .11 | .63 ± .10 | .298 |
| Total Number of Symptoms | 2.67 ± 3.26 | 6.08 ± 5.23 | .053† |
| Total Symptom Severity | 4.08 ± 5.32 | 11.50 ± 12.15 | .089† |

Values are means ± SD. EU, Euhydration protocol; HYP, Hypohydration protocol
† Statistical trend toward significance

*K-D test:* There were no statistically significant changes in the performance on theK-D test between trials but a statistical trend toward significance was observed in the average time to complete K-D test between protocols (*p* = .064) (Table 5).

Table 5. King-Devick Test Scores

| | EU | HYP | *P* value |
|---|---|---|---|
| Best (sec) | 42.00 ± 14.04 | 43.57 ± 13.62 | .110 |
| Average (sec) | 43.37 ± 14.00 | 45.29 ± 13.72 | .064† |

Values are means ± SD. EU, Euhydration protocol; HYP, Hypohydration protocol
† Statistical trend toward significance

*VOMS:* Hypohydration resulted in significantly more symptoms at baseline (*p* = .017), and after smooth pursuits (*p* = .015), horizontal saccades (*p* = .009), vertical saccades (*p* = .013), convergence (*p* = .003), horizontal vestibular ocular reflex (VOR) (*p* = .003), vertical VOR (*p* = .007) and visual motor sensitivity (*p* = .003) during VOMS testing. On the other hand, hydration state did not significantly affect symptom provocation following each assessment (Table 6). Horizontal saccades (*p* = .075) and vertical VOR (*p*

= .079) provoked more symptoms in a hypohydration trial but it was not statistically significant.

Table 6. VOMS Scores

| | EU | HYP | *P* value |
|---|---|---|---|
| Baseline | .38 ± .77 | 2.77 ± 3.17 | .017* |
| Smooth Pursuits | .54 ± .78 | 2.85 ± 2.94 | .015* |
| - Baseline | .15 ± .90 | .08 ± 1.19 | .808 |
| Horizontal Saccades | .46 ± .78 | 3.77 ± 3.92 | .009* |
| - Baseline | .08 ± .86 | 1.00 ± 1.63 | .075† |
| Vertical Saccades | .62 ± 1.04 | 3.46 ± 3.38 | .013* |
| - Baseline | .23 ± 1.17 | .69 ± 1.38 | .307 |
| Convergence | .46 ± .78 | 3.46 ± 2.82 | .003* |
| - Baseline | .08 ± .64 | .69 ± 2.10 | .345 |
| Convergence Distance (cm) | 1.86 ± 1.28 | 2.00 ± 1.20 | .762 |
| Horizontal VOR | 1.00 ± 1.29 | 3.92 ± 3.30 | .003* |
| - Baseline | .62 ± 1.12 | 1.15 ± 1.57 | .279 |
| Vertical VOR | .92 ± 1.44 | 4.38 ± 3.99 | .007* |
| - Baseline | .54 ± 1.27 | 1.62 ± 1.71 | .079† |
| Visual Motion Sensitivity | 1.23 ± 1.48 | 4.77 ± 3.37 | .003* |
| - Baseline | .85 ± 1.35 | 2.00 ± 2.80 | .190 |

Values are means ± SD. EU, Euhydration protocol; HYP, Hypohydration protocol
VOR, Vestibular Ocular Reflex

*Significant difference between EU and HYP

† Statistical trend toward significance

*Effort Assessments:* No significant difference was revealed on either Effort Questionnaire or NASA Task Load Index between the hydration states (Table 7).

Table 7. Effort Scores

| | EU | HYP | *P* value |
|---|---|---|---|
| Effort Questionnaire | 3.83 ± .39 | 3.92 ± .29 | .339 |
| NASA Task Load Index | | | |
| Mental Demand | 6.06 ± 2.22 | 5.72 ± 2.19 | .647 |
| Temporal Demand | 4.73 ± 2.21 | 4.78 ± 3.13 | .962 |
| Performance | 7.33 ± 1.97 | 7.55 ± 1.84 | .766 |
| Frustration Level | 2.13 ± 1.84 | 2.41 ± 3.08 | .687 |
| Effort | 6.02 ± 2.44 | 6.94 ± 1.91 | .258 |

Values are means ± SD. EU, Euhydration protocol; HYP, Hypohydration protocol

## Chapter 5: Discussion

This is the first study to investigate an isolated effect of mild hypohydration on neurocognitive, balance, and vestibular ocular motor function as well as mood.

In order to isolate the effect of hypohydration, 20 hours fluid restriction with an identical 30 to 45 minute workout performed 15 hours prior to trials was applied as our dehydration method. This exercise protocol allowed us to eliminate the influence of fatigue on concussion assessment tools and produced the desired level of hypohydration (> 1 % body mass reduction). Our participants achieved 2.13 ± 1.07 body mass loss and demonstrated mild hypohydration. We successfully controlled for confounding factors such as heat exposure, hyperthermia and fatigue.[26-31, 33] Effort level can also affect testing outcomes. We found no significant differences in Effort Questionnaire or NASA Load Index between trials. This suggests that our participants maintained effort in both trials.

*Neurocognitive function:* Neurocognitive function is a broad term used to describe different functions controlled by the brain and can be grouped into major categories including memory, attention, perception, psychomotor, language and executive functions.[59] In this study, SAC in SCAT3 and verbal memory, visual memory, visual motor and reaction time in ImPACT measured neurocognitive functions. No significant differences were observed between euhydration and hypohydration. It suggests that mild hypohydration did not significantly compromise neurocognitive performance in SCAT3 or ImPACT. The physiological relationship between hydration and neurological function is unclear. Hypohydration is an unpleasant condition and increases the level of cortisol as a stress response. Higher levels of cortisol can impair brain functions.[60] Arginine vasopressin and angiotensin II are also released in the body during hypohydration to maintain fluid balance. These hormones are known to affect neurotransmitters.[61, 62] Carboxylate anion glutamate and gamma aminobutyric acid are neurotransmitters that inhibit and promote neural activity. Elevations in the levels of these neurotransmitters have been observed during hypohydration.[63] There is a close association between neural activity and cerebral blood flow.[64] However, mild hypohydration does not change cerebral blood flow at rest.[65] This potentially explains why no significant declines in neurocognitive performance were observed in this study. The impact of hydration state on neurocognitive function is inconsistent in previous studies. The inconsistency in research is most likely due to methodological differences in dehydration procedures and neurocognitive assessments. Previous studies used exercise tasks, heat exposure or the combination of exercise and heat exposure to induce hypohydration.[13, 15, 16, 32] It has been shown that long-term exercise improves cognitive function[26-28] but fatigue produces a negative influence on cognition. [29-31] Hyperthermia can also cause cognitive deficits.[33] These different dehydration methods could contribute to varied findings. Differences in cognitive assessment tools could be another factor that generate different outcomes. Patel et al. (2007) performed SAC to examine the influence of hydration on neurocognitive function.[11] Our findings in SAC were consistent with theirs. However, they found visual memory impairment in computer-based neurocognitive test during hypohydration compared with euhydrated condition. Automated Neuropsychological Assessment Metrics (ANAM), which is also a common concussion assessment tool, was utilized as a computerized cognitive test in their study. The subjects in their study performed an aerobic exercise task only in a hypohydrated trial. The inconsistent findings were due to the differences in neurocognitive testing tool and dehydration method used. Iverson et al. (2003) reported reliable change confidence intervals in verbal memory, visual memory, visual motor and reaction time composite scores in ImPACT as follows; > 8 points, > 13 points, > 5 points and > .06 sec respectively.[66] Our findings suggested that neurocognitive assessments using SAC and ImPACT were not sensitive to hydration changes.

*Balance:* We did not find a significant difference between euhydration and hypohydration trials in postural control assessed by BESS and the tandem walk. There were higher error scores in BESS and slower time to complete tandem walk but these were not statistically significant and demonstrated similar scores to previously reported normative values.[67] Similarly, previous studies did not reveal BESS score differences between euhydrated and hypohydrated trials.[11] They added NeuroCom Sensory Organization Test (SOT) into their balance assessment batteries and found the increased performance in somatosensory component of SOT. However, subjects in their research study completed 45 minutes of exercise 30 minutes prior to testing. The exercise protocol could have activated postural muscles, which improve postural control performance. Postural control is achieved through vestibular, visual and proprioceptive inputs.[68] Balance problems are commonly reported among concussed patients.[69] Neural activity between central and peripheral nervous systems play a crucial role in maintaining posture.[68] As discussed above, the change in cerebral blood flow affects neural activity,[64] but cerebral blood flow is maintained during mild hypohydration.[65] Therefore, mild hypohydration did not impair the scores in BESS and tandem walk. Our findings suggest that balance performance was not negatively affected by hypohydration.

*Vestibular Ocular motor function:* Symptoms in VOMS differed significantly between conditions. The subjects reported more symptoms in baseline and all seven testing maneuvers during the hypohydrated trial. On the other hand, hypohydration did not have negative influence on symptom provocations or near point of convergence (NPC) distance. It is common that hypohydrated patients report mood change and negative symptoms such as headache, dizziness, nausea and fatigue.[11-23] In fact, we found that hypohydration produced more unpleasant symptoms (discussed later). Mucha et al. (2014) reported a positive correlation between VOMS symptoms and the Post-Concussion Symptom Scale.[70] Interestingly, the means of total VOMS symptoms in the hypohydrated condition were greater than the VOMS symptoms reported in concussed patients.[70] Patients rate headache, dizziness, nausea and fogginess after each VOMS assessment. Headache, dizziness and nausea are common symptoms in hypohydration.[9, 10] It may be a reason that the hypohydrated subjects in this study demonstrated higher symptom scores than the symptoms concussed patients reported in the previous study. More symptoms were reported in the hypohydrated trial compared with euhydration. However, there was no significant difference in NPC distance or symptom provocation, which is defined as baseline symptom scores subtracted from the symptom scores after each VOMS assessment. Vision and eye movements are controlled through complex systems in the brain.[71] It appeared that mild dehydration caused discomforts but did not change actual neural activity in the brain. Thus, VOMS did not significantly provoke symptoms or change NPC distance.

This suggests that VOMS symptom scale was sensitive to hypohydration but symptom provocation in VOMS and NPC were not affected by mild hypohydration.

*Mood:* Our findings were consistent with previous findings in mood disturbances.[11-23] In SCAT3, the subjects rated symptoms significantly higher and severe. There were statistical trends in both total number of symptoms and severity of symptoms in ImPACT comparing euhydrated protocol and hypohydrated protocol although statistical significant difference was not revealed. It is likely due to different symptom lists in these testing tools and small sample size in this study. Both SCAT3 and ImPACT symptom scales are consisted of 22 symptom questions. 18 out of 22 symptoms are very similar but ImPACT lists “sleeping more”, “sleeping less”, “numbness”, and “vomiting” instead of “don’t feel right”, “pressure in head”, “neck pain” and “confusion”. Our data suggests that the symptom scale in SCAT3 is more sensitive to hydration state. We did not have enough statistical power in this study because only 13 subjects participated. The small sample size may be one of the reasons that statistical differences were not noted in ImPACT symptom scales. With regard to the symptom scores in ImPACT, our findings showed that the symptoms reported during hypohydration was less severe than the post-concussion symptoms.[66] The mechanism of mood swings during mild hypohydration is unclear. Ganio et al. (2011) suggested that a hypothalamic neuron, which is responsible for body fluid regulation, might send signals to other regions of the brain that control mood during hypohydration.[19]

Mild hydration can occur during a sport practice or daily activity. It has been shown that athletes are habitually hypohydrated.[8] Our findings showed that mild hypohydration produced concussion-related symptoms. Health care providers should be careful when interpreting self-reported symptoms if hypohydration is suspected. Relying solely on symptom score is not a good clinical practice in assessing concussion. As the National Athletic Trainers' Association recommends,[3] multiple concussion testing tools should be used. Neurocognitive, balance, vestibular ocular motor performances in SCAT3, ImPACT, K-D test, and VOMS were not significantly affected by hydration state in our participants. Hypohydration would not change clinical decisions when performing these testing tools as baseline or post-injury assessments. However, performances for more than 80 % of outcomes were compromised with our participants in a hypohydrated state compared to when they were euhydrated. Clinicians should consider athletes' hydration status when performing baseline assessments and evaluating concussion in order to improve concussion management. Dehydration methods used in previous studies (e.g., heat exposure and exercise) have confounding effects on the outcomes. The isolated influence of hydration state on cognitive function, postural stability and mood had not been examined previously. In addition, there was no research studying vestibular ocular motor function during hypohydration. This research is also the first to utilize common concussion assessment batteries such as ImPACT, SCAT3, VOMS and King-Devick test as outcome measurements.

*Limitations:* We could not have enough statistical power in this study. Due to strict inclusion and exclusion criteria in order to examine the isolated effect of hypohydration on concussion testing batteries, only 13 subjects participated in our study. The small sample size can be a factor to detect the significant difference.

*Future study:* Further study is necessary to establish the influence of hypohydration on the outcomes in widely used concussion testing tools using a larger sample size. In addition, females should participate in future studies. The effect of hypohydration on cognition was different between gender.[13, 19] Females tend to be prone to hypohydration because of menstrual cycle. How hydration status affects the outcomes in concussion testing batteries should be studied to enhance concussion management and establish appropriate baseline values.

# Chapter 6: Conclusion

Our findings suggest that mild hypohydraion (~2%) can negatively alter mood but neurocognitive, balance and vestibular ocular motor functions are maintained. Further study is required to examine the influence of hypohydration on the performances using the same concussion testing batteries in a large sample size including females.

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# Appendix: Research Compliance Letter

UNIVERSITY OF ARKANSAS

*Office of Research Compliance*
*Institutional Review Board*

February 11, 2015

MEMORANDUM

| | |
|---|---|
| TO: | Satoshi Iida<br>Cory Butts<br>Caitlin Gallion<br>Evan Dobbs<br>Matthew Ganio<br>Brendon McDermott |
| FROM: | Ro Windwalker<br>IRB Coordinator |
| RE: | New Protocol Approval |
| IRB Protocol #: | 14-12-377 |
| Protocol Title: | *The Effect of Hypohydration on the Outcomes of Concussion Assessment Testing* |
| Review Type: | ☐ EXEMPT ☒ EXPEDITED ☐ FULL IRB |
| Approved Project Period: | Start Date: 02/10/2015 Expiration Date: 01/19/2016 |

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Your protocol has been approved by the IRB. Protocols are approved for a maximum period of one year. If you wish to continue the project past the approved project period (see above), you must submit a request, using the form *Continuing Review for IRB Approved Projects*, prior to the expiration date. This form is available from the IRB Coordinator or on the Research Compliance website (https://vpred.uark.edu/units/rscp/index.php). As a courtesy, you will be sent a reminder two months in advance of that date. However, failure to receive a reminder does not negate your obligation to make the request in sufficient time for review and approval. Federal regulations prohibit retroactive approval of continuation. Failure to receive approval to continue the project prior to the expiration date will result in Termination of the protocol approval. The IRB Coordinator can give you guidance on submission times.

**This protocol has been approved for 85 participants.** If you wish to make *any* modifications in the approved protocol, including enrolling more than this number, you must seek approval *prior to* implementing those changes. All modifications should be requested in writing (email is acceptable) and must provide sufficient detail to assess the impact of the change.

If you have questions or need any assistance from the IRB, please contact me at 109 MLKG Building, 5-2208, or irb@uark.edu.

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