Dehydration Increased Mitochondrial Fission and Autophagy Response to Resistance Exercise in Peripheral Blood Mononuclear Cells.

CASEY R. APPELL[1], NIGEL C. JIWAN[1,2], CARSON LEWIS[1], ISABELL R. TREVINO[1], RYANONEIL ELLIS[1], JALYN DUNLAP[1], ANDREW SCHINDEL[1], KARINA OLVERA[1], MIA URIEGAS[1], HUI-YING LUK[1]

[1]Department of Kinesiology and Sport Management, Texas Tech University, Lubbock, TX, USA

[2]Department of Kinesiology, Hope College, Holland, MI, USA

INTRODUCTION

- Dehydration, leading to hyperosmotic stress, is a physiological stressor which can trigger cellular shrinkage, oxidative stress, and even DNA damage potentially.
- A growing body of *In-Vitro* evidence indicates that hyperosmotic stress triggers cellular stress responses, including mitochondrial dysfunction and the activation of autophagy, a process of cellular self-degradation.
- Peripheral blood mononuclear cells (PBMCs), a heterogeneous population including monocytes and lymphocytes, are crucial drivers of immune responses and serve as valuable biomarkers for assessing immune system status, particularly following physiological stressors like exercise.
- LPS stimulated PBMCs exposed to hyperosmotic stress In-Vitro release pro-inflammatory cytokines, molecules used to modulate immune function.
- Proper mitochondrial dynamics and autophagic flux are vital for maintaining cellular homeostasis and immune cell function, with dysregulation potentially exacerbating pro-inflammatory responses.
- Despite the known individual effect of resistance exercise on cellular stress, the combined impact of dehydration on PBMC stress responses, specifically mitochondrial fission and autophagy, remains underexplored.
- Therefore, this study aimed to examine the effect of dehydration on PBMCs' stress responses, including mitochondrial fission and autophagy, after resistance exercise in young, trained men.

PURPOSE

- To examine the effect of dehydration on peripheral blood mononuclear cells (PBMCs) stress responses after resistance exercise (RE) in young, trained men.

METHODS

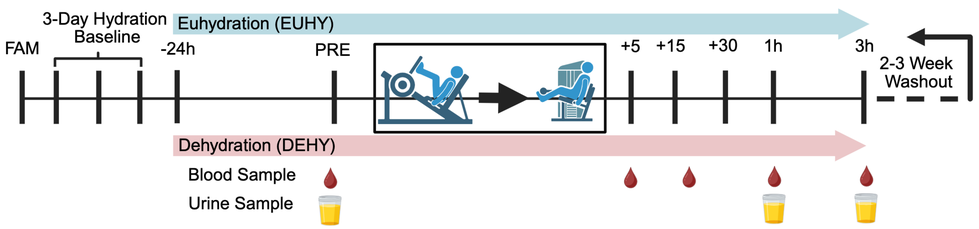


Figure 1. Study Design

Fluid Restriction Diet

- EUHY: Adequate fluid intake to maintain hydration 24h prior to exercise.
- DEHY: No fluid consumption 24h prior to exercise (~2% body mass loss). Participants avoided foods with high water content.

Resistance Exercise

- Bilateral leg press and knee extension exercises.
- 5 sets of 10 repetitions with 2 minutes of rest between sets.
- 80% of 1-RM for each set and exercise.

Analyses

- PBMC protein content analyses measured by Western Blot.
- Plasma osmolality (P_{osmo}) measured by Osmometer.
- Urine specific gravity (USG) measured by Digital USG Refractometry.

Statistical Analyses

- Data was analyzed using a condition x time repeated measures ANOVA.
- Alpha level was set to <0.05
- All data are presented as means ± SD.

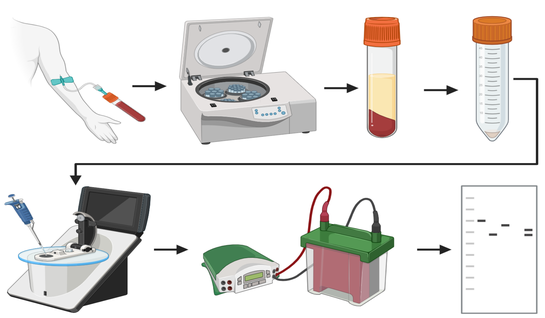


Figure 2. PBMC Protein Content Analyses

RESULTS

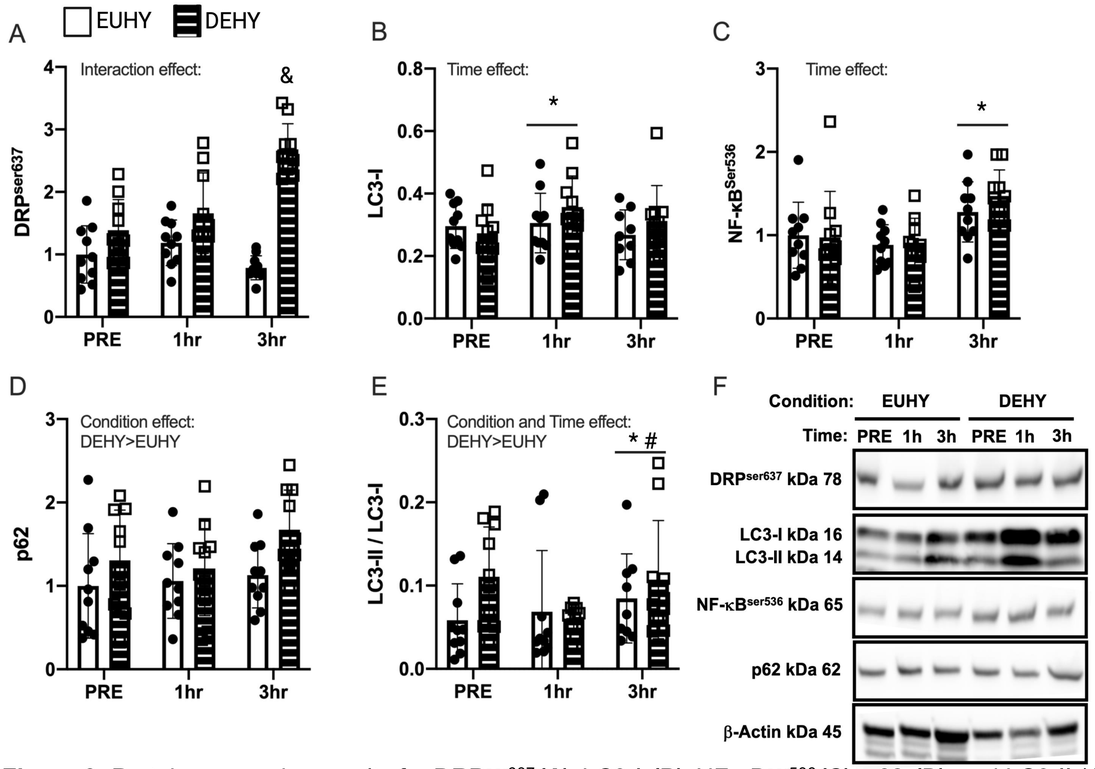


Figure 3: Protein expression results for DRP^{ser637} ***(A)***, LC3-I ***(B)***, NF-κB^{ser536} ***(C)***, p62 ***(D),*** and LC3-II / LC3-I ratio ***(E)***. Data from 1h and 3h were normalized to the EUHY PRE. Representative blots ***(F)*** of PRE, 1h, and 3h target protein contents and the corresponding housekeeping protein (β-actin). Molecular weight marker (kDa). *p <0.05 vs. PRE. #p <0.05 vs. 1h. &p <0.05 vs. EUHY.

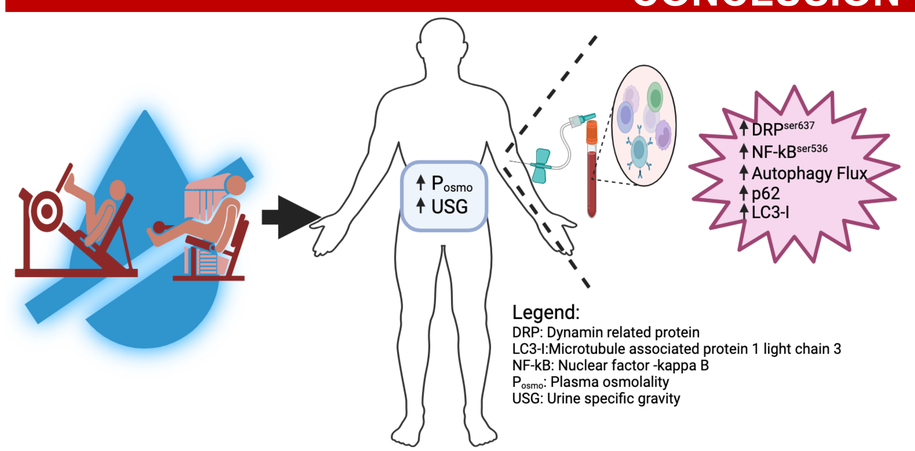
Posm (mmol/kg)	EU	DE
PRE	282±4	295±8
1h	283±4	296±4
3h	281±2	295±6

Table 1. Plasma Osmolality (Posm). Values are mean ± SD.

USG	EU	DE
PRE	1.010±0.004	1.026±0.005
1h	1.013±0.004	1.026±0.003
3h	1.007±0.006	1.026±0.003

Table 2. Urine specific gravity (USG). Values are mean ± SD.

CONCLUSION



- PBMCs stress responses were elevated in young, trained men exposed to mild dehydration during RE.
- Although the activation of the inflammatory marker NF-κB did not differ between conditions, mitochondrial fission (DRP1^{ser637}) and autophagy (autophagic flux) were higher under dehydration.
- These findings suggest that acute dehydration adds an additional stressor during RE, amplifying fragmentation of the mitochondrial network and protein degradation in PBMCs.

PRACTICAL APPLICATIONS

- A proper PBMCs mediated inflammatory response to RE is vital for muscle recovery.
- Elevated fragmentation of the mitochondrial network and protein degradation has been shown to exacerbate the pro-inflammatory PBMCs response in-vitro.
- Further, an exacerbated pro-inflammatory response impairs muscle recovery in-vitro.
- These preliminary data are the first to suggests that proper hydration could minimize stress in inflammatory cells (PBMCs) in young, trained men.
- However, the effect of dehydration on PBMCs response and its effect on muscle recovery remains unknown.