The purpose of this study was to determine if ENT can:

1. Increase performance in the heat
2. Reduce paracellular permeability
3. Suppress the systemic inflammatory response
4. Increase cell proliferation and accelerate recovery

We hypothesized that Enterade® (ENT), an amino acid-based oral rehydration solution, will protect the gut from increased permeability during EHS, mitigating the systemic inflammatory response during a variety of stressors.

**INTRODUCTION**

- The adverse sequelae following exertional heat stroke (EHS) is hypothesized to be a consequence of endotoxin leakage secondary to increases in gut permeability.
- Oral administration of specific amino acids has been shown to decrease endotoxin leakage, and suppress the inflammatory response during EHS, tightening the mucosal barrier, reducing paracellular permeability, and decreasing endotoxin leakage, and suppressing the inflammatory response.
- The purpose of this study was to determine if ENT can:
  - Increase performance in the heat
  - Reduce paracellular permeability
  - Suppress the systemic inflammatory response
  - Increase cell proliferation and accelerate recovery

**METHODS**

**Study Design**

- Implant Temperature Transmitters
- Free Running Wheels Added
- Familiarization Sessions
- Randomization
- EHS Protocol
- Exercise Control

**EHS Protocol**

**RESULTS**

**Thermoregulatory Performance**

<table>
<thead>
<tr>
<th></th>
<th>EHS ENT</th>
<th>EHS H2O</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial weight (g)</td>
<td>27.8 ± 1.7</td>
<td>27.3 ± 1.4</td>
<td>0.1027</td>
</tr>
<tr>
<td>Performance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dehydration (%)</td>
<td>9.4 ± 2.1</td>
<td>9.3 ± 1.7</td>
<td>0.8177</td>
</tr>
<tr>
<td>Max speed (m/min)</td>
<td>5.9 ± 1.1</td>
<td>5.8 ± 0.1</td>
<td>0.5742</td>
</tr>
<tr>
<td>Distance (meters)</td>
<td>707.8 ± 251.5</td>
<td>693.9 ± 180</td>
<td>0.7595</td>
</tr>
<tr>
<td>Thermal Area</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tc Max (°C)</td>
<td>42.2 ± 0.2</td>
<td>42.2 ± 0.2</td>
<td>0.9673</td>
</tr>
<tr>
<td>Time to Tc Max (min)</td>
<td>160.9 ± 38.8</td>
<td>155.5 ± 27.7</td>
<td>0.8463</td>
</tr>
<tr>
<td>Thermal Load</td>
<td>552.5 ± 89.5</td>
<td>545.7 ± 82.7</td>
<td>0.7098</td>
</tr>
<tr>
<td>Ascending Thermal Area (°C)</td>
<td>523.7 ± 88.2</td>
<td>519.0 ± 79.8</td>
<td>0.7885</td>
</tr>
<tr>
<td>Descending Thermal Area (°C)</td>
<td>26.9 ± 6.3</td>
<td>26.5 ± 5.5</td>
<td>0.7739</td>
</tr>
<tr>
<td>Hyperthermia Severity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to Tc Minimum (min)</td>
<td>129.3 ± 34.6</td>
<td>136.2 ± 39.7</td>
<td>0.6159</td>
</tr>
<tr>
<td>Tc Minimum (°C)</td>
<td>32.9 ± 0.4</td>
<td>32.1 ± 0.8</td>
<td>0.0020**</td>
</tr>
<tr>
<td>Hypothermia depth (°C)</td>
<td>33.3 ± 0.3</td>
<td>32.5 ± 0.8</td>
<td>0.0024**</td>
</tr>
<tr>
<td>Hypothermia duration (min)</td>
<td>186.9 ± 47.3</td>
<td>243.6 ± 42.3</td>
<td>0.0012**</td>
</tr>
</tbody>
</table>

**Small Intestine Histology**

**Gut Permeability**

**Circulating Biomarkers**

**CONCLUSIONS**

- ENT decreases EHS severity as indicated by depth and duration of hypothermia.
- ENT mitigates increases in gut permeability.
- ENT decreases EHS severity by reducing the depth of hypothermia.
- ENT decreases paracellular permeability as evidenced by conductance, FITC dextran, and histology.
- Circulating markers of organ injury and the innate immune response were similar between ENT and H2O throughout the course of recovery.
- These results suggest that ENT improves Tc regulation during EHS recovery, but this dosage had no effect on the systemic inflammatory response that is characteristic of EHS at select time points.

**Key Organ Injury Markers**

- ENT mitigates increases in gut permeability
- ENT attenuates minimum Tc reached, hypothermia depth, and hypothermia length.
- ENT decreases paracellular permeability as evidenced by conductance, FITC dextran, and histology.
- Circulating markers of organ injury and the innate immune response were similar between ENT and H2O throughout the course of recovery.
- These results suggest that ENT improves Tc regulation during EHS recovery, but this dosage had no effect on the systemic inflammatory response that is characteristic of EHS at select time points.

**Key Cytokines**

- ENT decreases EHS severity as indicated by depth and duration of hypothermia.
- ENT mitigates increases in gut permeability.
- ENT decreases paracellular permeability as evidenced by conductance, FITC dextran, and histology.
- Circulating markers of organ injury and the innate immune response were similar between ENT and H2O throughout the course of recovery.
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**Key Chemokines**

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- These results suggest that ENT improves Tc regulation during EHS recovery, but this dosage had no effect on the systemic inflammatory response that is characteristic of EHS at select time points.

**Author views not official US Army or DoD policy.**