Resistance to multi organ damage after hemorrhagic shock induced ischemia/ reperfusion in arctic ground squirrels

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INTRODUCTION

• Worldwide hemorrhagic shock is the number one cause of death in trauma patients. The majority of these due to multi organ dysfunction syndrome (MODS) and during hemorrhagic shock (HS), the body undergoes global ischemia as blood pressure drops below the threshold at which tissue can be adequately perfused with blood.
• Resistance to ischemic injury is a characteristic of hibernating mammals, including ground squirrels.
• There is debate on if this resistance is dependent on hibernation season or if it is an intrinsic property of the organism.

QUESTION: Are AGS protected from HS-induced ischemia reperfusion (I/R) injury on the whole organism and tissue-specific levels and if any protection is dependent upon their hibernation season.

METHODS

Figure 1: HS isobaric procedure

![Diagram of HS isobaric procedure](image)

Table 1: Components of analysis

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiological</td>
<td>HS: Blood; temperature (head, core, limb); HR; body weight, blood glucose, blood lactate, complete blood count (CBC).</td>
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<tr>
<td>Blood chemistry</td>
<td>Blood urea nitrogen (BUN), creatinine, bicarbonate, creatine phosphokinase (CPK), lactate dehydrogenase (LDH), aspartate aminotransferase (AST), and alanine aminotransferase (ALT).</td>
</tr>
<tr>
<td>Histopathology</td>
<td>Heart, liver, intestine, kidney, spleen, and lung.</td>
</tr>
<tr>
<td>Cytokine and immunochemistry</td>
<td>TGF-β, IL-1β, IL-6, TNF-α, IL-12, IFN-γ, gamma.</td>
</tr>
</tbody>
</table>

Table 2: AGS seasonal group parameters

<table>
<thead>
<tr>
<th>Season</th>
<th>Hemorrhage (n=30)</th>
<th>Survival (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Summer/Euthermia</td>
<td>15 mm, 4°C</td>
<td>15 mm, 37°C</td>
</tr>
<tr>
<td>Winter/Interbout Arousal</td>
<td>15 mm, 3°C</td>
<td>15 mm, 37°C</td>
</tr>
</tbody>
</table>

RESULTS

Figure 2: Rats do not survive 18 hrs after HS while AGS survive a minimum of 72 hrs afterward

![Graph showing survival after hemorrhagic shock](image)

Figure 3: AGS recover to normal behavior by 18 hrs after HS

![Graph showing AGS recovery to normal behavior](image)

Figure 4: AGS do not show early indicators of organ damage in the kidney (creatinine) or liver (ALT, AST) regardless of hibernation season

![Graph showing creatinine and ALT/AST levels](image)

Figure 5: Metabolic shift indicated by an increase in lactate production and negative base excess occurs in rats during and after HS but not in AGS

![Graph showing plasma lactate to glucose ratio and base excess](image)

Figure 6: Circulating plasma cytokine levels do not increase in AGS after HS

![Graph showing plasma cytokine levels](image)

CONCLUSIONS

Independent of hibernation season, AGS were resistant to HS induced I/R injury on the whole organism and tissue specific level.

Both euthermic and interbout arousal AGS can survive without apparent physiological deficit for 3 days after HS at euthermic body temperature when blood drop corresponds to an MAP of 25 mmHg (~ 50% total blood volume).

Maintain a high base excess during and after HS

Do not show blood serum markers for organ damage

Do not have systemic inflammatory cytokine response after HS I/R injury.

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We would like to thank UAF Veterinary Services, UAF Veterinary Diagnostics, and Fairbanks Memorial Hospital for assistance with sample analysis.

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