Metabolic Control as a Strategy for Payload Cost Reduction and Mitigation of Negative Space Environmental Factors

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As human presence in space will likely extend to the Moon and beyond, such exploration missions will involve significant risks of accidents, system failures, and various life-threatening emergency situations. The ability to put space explorers into a temporary hypo-metabolic state using metabolic control technologies would enhance our ability to manage these risks. Reversible arrest of essential life processes would radically reduce astronaut needs for life support and produce extraordinary resistance to environmental stress, such as radiation exposure and low-gravity. It can also solve many medical problems including diseases and physical injury over a long period in space.

Despite promising avenues of these enquiries, the mechanism of inducing such reversible hypometabolic state in non-hibernated animals is not yet fully understood (Blackstone, et al., 2005; Tøien, et al., 2011; Haouzi, et al., 2008). We developed the methodology to achieve metabolic control, which allows the metabolism of non-hibernated animal model system (mice) to be reduced to a minimum level for a significant time and subsequent restoration to normal level with no apparent effect on physiology or neurological function. In order to demonstrate the potential application of the metabolic control technology we have engineered a hypometabolic chamber with a range of life-monitoring equipment.

Figure 1. Schematic presentation of the hypometabolic system used in this study.
for high-throughput testing of hypometabolic parameters and conditions that enable reversible induction of a state of suspended animation in mice (Figure 1). The automated monitoring system is responsible for initiation, maintenance, and termination of the stasis through the administration of hypometabolic agents and providing immediate short-term monitoring and control.

C57BL/6J male mice from Jackson Laboratories were used in this study. The animals were 6 weeks of age at the time of experimentation and weight 20-30 g. Two groups of 5 animals (control and experimental) were implanted with biotelemetry transmitters to continuously measure body temperature and cardiac activity. Induction of the hypometabolic state in mice was carried out by using a custom designed atmospheric chamber. Following short adaptation in air atmosphere mice was exposed to 80 ppm H2S air mixture at a constant pressure and flow rate 1L/min to induce hypometabolic state (Blackstone et al., 2005). At this point the environmental temperature was decreased gradually using programmable temperature control software from ambient temperature to 15°C. Hypometabolic state was evident by reduction in metabolic rate and drop in oxygen consumption and carbon dioxide output. After 10 hours of exposure to H2S the atmosphere in the chamber was substituted with air and mice were returned to room temperature. The recovery to the normal state was monitored by metabolic rate and core body temperature returning to normal. After this stage animals were placed in a standard vivarium cage for 30 days observation period. All animal experiments were performed in strict accordance with National Institutes of Health guidelines, and animal protocols were approved by the IACUC at Ames Research Center.

After exposure to the hypometabolic mixture, core body temperature drops from 37°C to 15°C over 8.5 hours of the gas exposure (Figure 2) leading to substantial reduction in rate of all biochemical reactions in organism.

The mouse initially started at a heart rate of 762 beats/minute, then dropped to as low as 120 beats/minute after 10 hours (Figure 3) – a 75% drop in heart rate.

![Core body temperature of mice exposed to H2S using the same protocol and recovered from the stasis at different times. Control mice were not exposed to H2S. Each data point is average of three experiments.](image1)

![Figure 3. Heart rate recorded at different body temperatures. (a) 37°C; (b) 15°C; (c) 37°C, after recovery from the stasis.](image2)
to less than 5 breaths per minute, demonstrating reduction in metabolism more than 94%. After recovery from the stasis, none of the hypometabolic animals displayed any behavior deficits over 3 months of observation. We have shown that recovery from the intentionally induced hypometabolic state may be 30% better than in natural hibernators (~47% lethality) when the kinetics of induction, extension and recovery from this state are optimized.

Our data provide basis for subsequent animal studies and novel approaches in further extension of this state and development of continuous external monitoring and modification of metabolic conditions. Despite the obvious limitations of H\textsubscript{2}S for induction of hypometabolism in large animals, such as sheep (Haouzi et al., 2008), its application on small animals allows investigation of key underlying mechanisms and consequences of metabolic alteration in non-hibernated animals regardless of stasis protocol. Some other potential beneficial outcomes of the metabolic reduction, such as increase in life span, resistance to ionized radiation, low gravity and many pathogenisities are currently under investigation.

Investment in a program of research to define the optimum methods for achieving metabolic control in larger animals is needed at this time, in order to demonstrate application of a metabolic control system within deep space mission architecture as a potentially enabling technology.

**REFERENCES**

