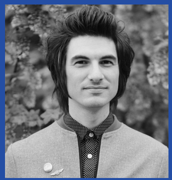

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Adapting synthetic torpor to spaceflight scenarios: Seldom-discussed challenges

Introduction

Synthetic torpor (abbr. ST) | a state of reversible metabolic depression that is artificially induced, typically in animals that are not capable of entering *natural* torpor (abbr. NT)

Forms of synthetic torpor can be induced using different compounds, including: N6-cyclohexyladenosine (CHA), 5'-AMP, muscimol, H_2S, T1AM/TH, and pyruvate

Synthetic torpor could theoretcially benefit human spaceflight in two main ways:

Health benefits
- Space radiation protection
- Microgravity protection

Mission benefits
- Reduced resource requirements for crew
- Reduced mass, volume and power demands

ST is in an early development stage, and most research efforts have focused on induction techniques.

The many downstream challenges of adapting ST to spaceflight scenarios have received less attention.

Challenges

Here are 5 challenges related to ST's potential spaceflight benefits and viability that should be discussed at this early development stage.

Does synthetic torpor convey the same space-related protective effects as natural torpor?

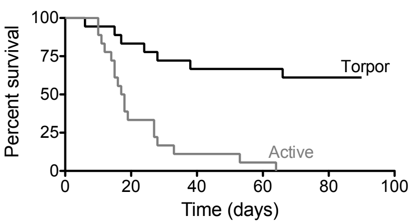

Fig. 1. Natural torpor enhances radiation resistance. Percent survival for 13-lined ground squirrels irradiated while in active (grey) or torpid (black) metabolic states at Day 0 with ^{60}Co at 1250 rad. Adapted from ref. 1.

NT enhances radiation resistance (**Fig. 1**), and hibernating animals' bones and muscles are relatively impervious to disuse (**Figs. S1, S2**).

Are these protective mechanisms related to torpor per se or to some other hibernation-related adaptation? If the latter, these additional mechanisms may need to be incorporated into ST.

How long can animals safely be held in synthetic torpor for?

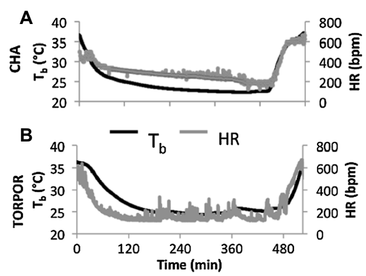

Fig. 2. A single CHA injection induces ~8 h of ST in mice. (A) CHA-induced ST, (B) diet-induced NT, each with similar T_b and HR trends. From ref. 2.

Long-term ST will be important to spaceflight torpor. So far, ST has been held for up to ~8 h in mice (**Fig. 2**).

Long-term ST will likely require biochemical/physiological processes to be held in a new steady state.

However, long-term ST will be complicated by serial administration of ST induction agent and metabolic fuels (eg., TPN) to avoid fuel exhaustion.

Do long-term synthetic torpor bouts require interbout arousals?

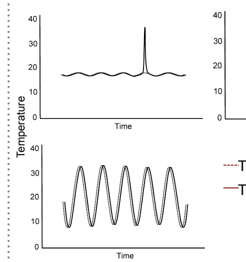

Fig. 3. Arousals appear to be temperature-dependent. Hibernating lemur arousal trends as a function of 3 different T_a trends. From ref. 3.

Most NT animals periodically arouse from torpor throughout the winter (**Fig. S3**). Exceptions are animals whose T_b remains, or periodically (and passively) rises, above 30°C (**Fig. 3**).

Housing ST animals/crewmembers at T_b ~31°C could eliminate incorporating IBAs in ST bouts, while still enabling a deep metabolic depression. >30°C would also avoid cardiac arrhythmias that develop in non-NT animals at T_b <30°C.

How does synthetic torpor affect cognition during and following the torpor bout?

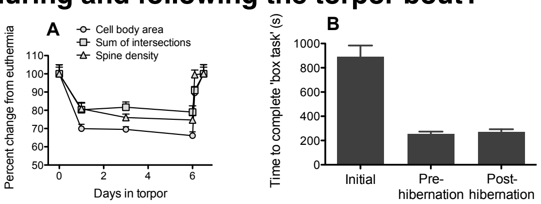

Fig. 4. Natural torpor affects neural architecture and may or may not affect cognition. (A) Torpor effects on neural structure in ground squirrels (adapted from ref. 4). (B) Hibernation effects on memory in marmots (adapted from ref. 5).

NT (specifically temperature) affects neural structure (**Fig. 4A**), impairing cognition in some animals (**Fig. S3**) but not others (**Fig. 4B**).

Cognitive states during and following ST bouts will need to be understood to ensure crewmember performance is not jeopardized.

What demands will synthetic torpor infrastructure place on spacecraft capacities?

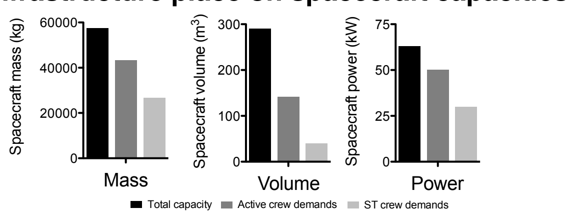

Fig. 5. Synthetic torpor may reduce demands on spacecraft capacities. Spacecraft capacities and active crew demands based on Mars DRA 5.0 specifications (refs. 6, 7). Estimated ST crew demands based on a ST T_b of 31°C, an overall Q_{10} of metabolic rate of 2.5, and a resulting 40% depression of metabolic rate. See Supplementary Material for details.

Demands of an ST crew on spacecraft capacities (**Fig. 5**) will likely vary depending on many factors, including:

- Depth of metabolic depression
- ST agent and administration method
- Torpor-arousal cycle

The Upshot

1. It is currently possible to induce ST in animals for at least 8 h.
2. While this duration may not be spaceflight-relevant, it is sufficient to begin testing basic principles of ST's application to spaceflight.
3. **These tests should be carried out soon to discern whether ST's theoretical benefits to spaceflight are realizable.**

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References

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