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Thermoregulation and nesting material in laboratory mice

Mouse nesting material recommendations from the current scientific literature

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The Guide and thermoregulation

- "In general, dry-bulb temperatures in animal rooms should be set below the animals' LCT to avoid heat stress. This, in turn, means that *animals should be provided with adequate resources for thermoregulation (nesting material, shelter) to avoid cold stress*." – Ch 3, p 43

- "A number of species, most notably rodents, exhibit a *clear preference* for specific materials (Blom et al. 1996; Manser et al. 1997, 1998; Ras et al. 2002), and *mice provided with appropriate nesting material build better nests* (Hess et al. 2008)." – Ch 3, p 68

Cold stress

General terms

- What does “stress” actually mean?
  - **Comfort** – homeostasis maintained with no additional resource use
  - **Stress** – homeostasis maintenance requires resource allocation
  - **Distress** – homeostasis cannot be maintained without compromising other biological functions

Feral Cats Ireland

Moberg 1999

How can we assess mouse cold stress?

Physiological measures

- Male C57BL/6 mice show ↑ anti-inflammatory, ↓ pro-inflammatory cytokine response to influenza when housed at 30° C than at 26° C or 22° C (Jhaveri et al 2007)
- BALB/c mice use less brown fat thermogenesis when supplied with nesting material (Gaskill et al 2013a)
- BALB/c and C57BL/6 mice in breeding pairs housed with nesting material weaned an average of 11 more pups over 6 months; those pups were also, on average, ~1.25g heavier (Gaskill et al 2013b)
- Mice (incl SCID, NUDE, BALB/c, and C57BL/6) housed at thermoneutrality showed decreased tumor growth and metastasis rates (4 diff types of tumor) when housed at thermoneutrality (Kokolus et al 2013)
- Male C57BL/6 mice housed at standard temps use 3 times their resting metabolic requirements at thermoneutrality. This is equivalent to a human naked at 5° C or walking 100 km/day (Fischer et al 2017)

How can we assess mouse cold stress?

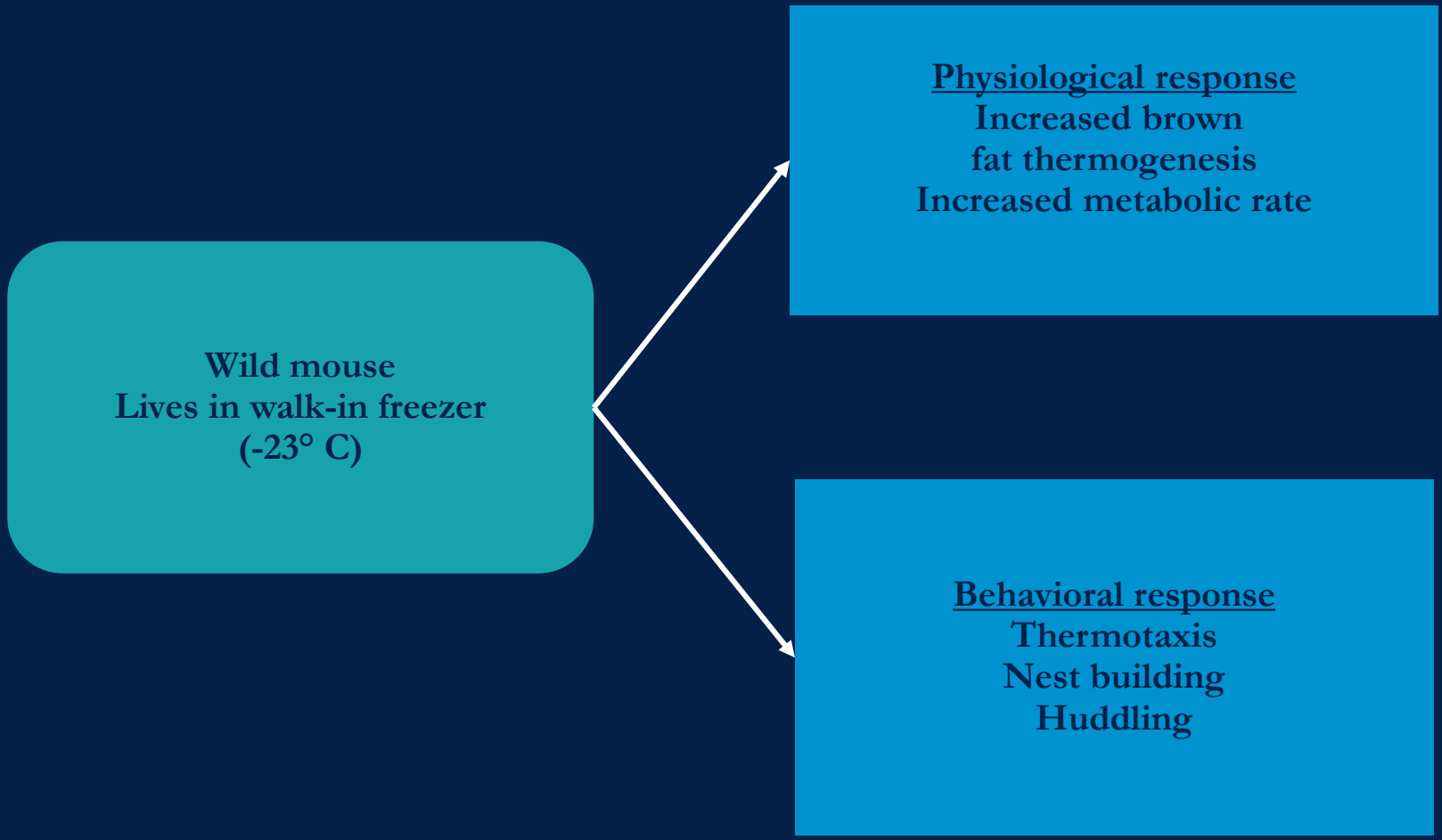
Behavioral measures

- C57BL/6 mice of both sexes given a choice between 20/25/30° C spent the majority of their time in 30° C. More inactive and maintenance time was spent there, too (Gaskill et al 2009)
- C57BL/6 mice provided with 8g of nesting material doubled the amount of time they spent in 20° C, but still spent more than 50% of their time in 30° C (Gaskill et al 2011)
- BALB/c female mice housed in a thermocline spent the majority of their time during the day in the 35-39° C end and engaged in very little nest building there (Gordon et al 2014)

Why are mice cold?

- Large surface area: volume ratio – loses heat quickly
  - Heavier mice, like CD-1s, are slightly less affected
- Ventilated caging?
  - Studies have shown mice find high IVC rates aversive (Baumans et al 2002) and IVC increases brown fat thermogenesis (David et al 2013)

How do they cope?



How can they cope?

Modifiers of coping mechanisms in the laboratory

- Opportunity
  - No chance for thigmotaxis
  - No huddling if housed singly
- Ability
  - Some mouse strains are “better” nesters than others
  - Physical condition
- Materials
  - Some nesting materials make higher scoring nests than others
  - Material durability, esp with 3 week cage changes
  - Bedding that can be integrated into the nest can modify nest score
  - Amount of material provided affects nest score

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Mouse nests

What's a nest score, anyway?

- Nest scoring is based on shape of nest
- Higher scoring nests -> higher in-nest temperature (Gaskill et al 2013a)
- Decreases in nest scores can indicate illness and/or pain (Rock et al 2014, Hager et al 2015, Gaskill and Pritchett-Corning 2016)

Gaskill et al 2013a

Nest scoring

Hess et al 2008

Score	View from above	View from side
1		
2		
3		
4		
5		

Figure 2. Sample nests and their corresponding scores.

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Mouse nests

What enables high nest scores?

- Type of material
  - More naturalistic (shredded paper) -> higher nest scores than less naturalistic (pressed cotton) (Hess et al 2008)
- Amount of material matters
  - Mice in static cages need at least 8-10g of material to build thermally insulating nests (Gaskill et al 2012)

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Current approach

- Vast majority of mice housed socially
- Majority of mice housed in IVC caging
- Vast majority of mice housed on paper chip bedding
- All cages receive some form of nesting material unless there is an IACUC approved protocol
- “Standard” is 1 Nestlet (~2.6g) per cage
  - Not uniform across facilities or rooms
  - Some use shredded paper, esp with nudes
- Sentinel mice receive 2-3 Nestlets

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Example cages

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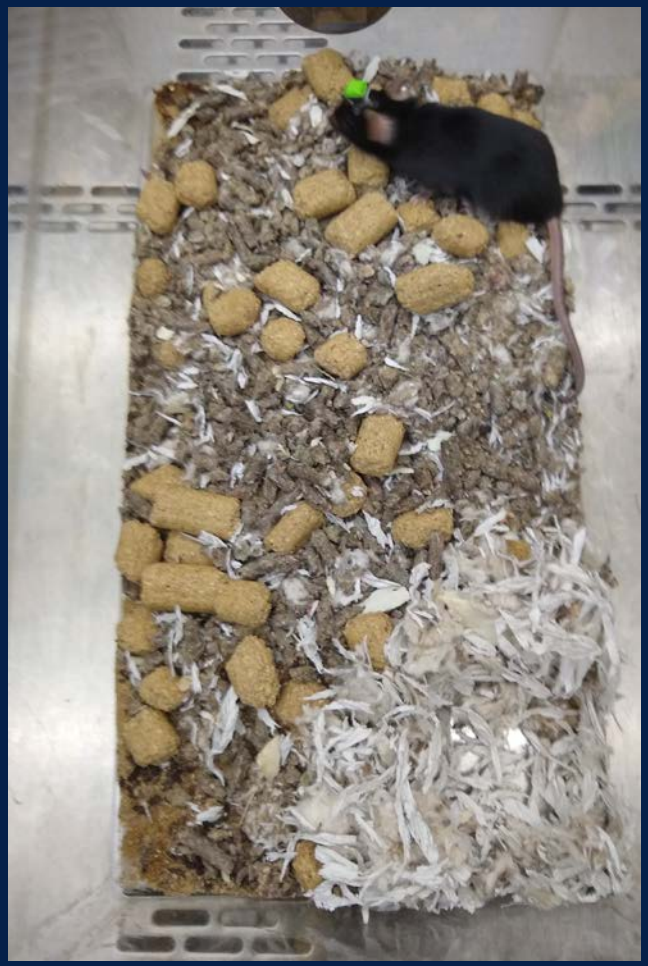
Example cages



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Recommendations

- Strongly recommended
  - Increase nesting material to 8g per cage
  - Automatically supply additional nesting material (up to 10g) to singly housed mice, including sentinels
  - Prefer shredded paper to compressed cotton
  - Transfer nesting material at cage change

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Larger scale potential improvements

Robinson-Junker et al 2016

- Consider using bedding with greater insulating properties/that can be incorporated into the nest
  - Also provides further opportunities to engage in natural behaviors (foraging, sorting, processing)

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