

NON – SHIVERING THERMOGENESIS IN NEONATES: THE HIDDEN MECHANISM OF THERMAL ADAPTATION

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Abstract

Thermoregulation is an important physiological challenge for neonates because they have a high surface-area-to-body-mass ratio, limited energy reserves, and an immature ability to regulate body temperature. Unlike adults, newborns have a limited capacity for effective shivering and therefore depend on non-shivering thermogenesis (NST) to maintain body temperature. Brown adipose tissue (BAT) is the major site of NST and produces heat primarily through mitochondrial uncoupling protein 1 (UCP1). In addition, skeletal muscle can contribute to NST through mechanisms involving sarcolipin (SLN)-mediated regulation of the sarcoplasmic reticulum Ca^{2+} pump SERCA. Other proposed mechanisms include creatine cycling, lipid cycling, and mitochondrial proton leak. Cold exposure activates the sympathetic nervous system, particularly norepinephrine-mediated pathways, which stimulate thermogenic tissues and increase metabolic heat production. Understanding these mechanisms is important for explaining neonatal adaptation to the extrauterine environment and for preventing cold stress and hypothermia in newborn animals and humans.

Keywords: Neonate, thermoregulation, non-shivering thermogenesis, brown adipose tissue, UCP1, sarcolipin, SERCA, skeletal muscle, cold stress

Introduction

Birth marks a profound transition from the protected intrauterine environment to the external world. While the fetus develops within a relatively warm and thermally stable uterus, the newborn is suddenly exposed to a much cooler surroundings and must rapidly establish effective mechanisms to maintain its core body temperature. This challenge is especially significant in neonates because of their high surface-area-to-body-mass ratio, relatively thin skin, limited subcutaneous fat stores, and immature thermoregulatory mechanisms. Consequently, neonatal survival depends on the rapid activation of heat-conserving and heat-producing mechanisms immediately after birth.

Maintenance of body temperature depends on a balance between heat production and heat loss. Heat can be generated by several mechanisms, including voluntary and

involuntary muscular activity and metabolic processes occurring in specialised tissues. In adults, shivering is an important response to cold exposure. Neonates, however, have a limited ability to produce sufficient heat through shivering. Consequently, they rely heavily on non-shivering thermogenesis.

Non-shivering thermogenesis refers to the generation of heat through metabolic processes without the characteristic rapid muscular contractions associated with shivering. Brown adipose tissue has traditionally been regarded as the principal site of NST in mammals. However, increasing evidence says that skeletal muscle and other tissues may also participate in this process. These mechanisms provide an important means of converting stored chemical energy into heat and thereby protecting the neonate from hypothermia.

Brown adipose tissue and ucp1-mediated thermogenesis

Brown adipose tissue is a specialised thermogenic tissue containing numerous mitochondria. Its ability to produce heat is primarily associated with uncoupling protein 1 (UCP1), which is located in the inner mitochondrial membrane.

Under normal conditions, mitochondria generate ATP using energy stored in a proton gradient across the inner mitochondrial membrane. UCP1 provides an alternative pathway for protons to cross this membrane. Consequently, the energy stored in the proton gradient is dissipated as heat rather than being used entirely for ATP synthesis.

Cold exposure activates the sympathetic nervous system and increases the release of norepinephrine at BAT. This stimulates β -adrenergic signaling and promotes the mobilization of fatty acids from triglyceride stores. Fatty acids provide substrates for mitochondrial metabolism and also contribute to activation of UCP1. The resulting increase in mitochondrial activity produces substantial amounts of heat.

This mechanism is particularly important in newborn mammals because BAT provides a rapid source of metabolic heat when environmental temperature falls.

Muscle-based non-shivering thermogenesis

Although BAT has traditionally received the greatest attention, skeletal muscle can also contribute to non-shivering heat production. This is especially interesting because skeletal muscle represents a large proportion of body mass in many mammals and therefore has considerable potential for energy expenditure.

One of the best-studied muscle mechanisms involves the interaction between sarcolipin (SLN) and sarcoplasmic/endoplasmic reticulum Ca^{2+} -ATPase (SERCA).

SERCA handles transporting Ca^{2+} from the cytoplasm back into the sarcoplasmic reticulum. This process requires ATP and is essential for normal muscle relaxation following contraction. Sarcolipin is a small membrane-

associated protein that interacts with SERCA and changes its activity.

When SERCA is influenced by sarcolipin, ATP hydrolysis can continue while Ca^{2+} transport becomes less efficient. Consequently, the muscle cell consumes additional ATP without producing an equivalent amount of useful mechanical work. The energy associated with this increased ATP utilization is dissipated as heat.

This process is commonly described as futile Ca^{2+} cycling and represents an important proposed mechanism of muscle-based NST.

(Importantly, sarcolipin should not be considered a hormone that is simply released into the circulation during cold exposure. It is a protein associated with the muscle membrane, and changes in its expression, regulation and interaction with SERCA can influence thermogenic activity.)

Creatine cycling and other thermogenic mechanisms

In addition to UCP1 and SLN-SERCA-mediated thermogenesis, other metabolic processes may contribute to NST. One such mechanism involves creatine cycling. Repeated conversion between creatine and phosphocreatine can consume ATP and increase energy expenditure. When this energy is not efficiently converted into useful mechanical work, a proportion can be dissipated as heat.

Lipid cycling has also been proposed as another contributor to thermogenesis. Repeated breakdown and re-synthesis of lipids require metabolic energy and can therefore increase heat production. Similarly, mitochondrial proton leaks that occur independently of UCP1 may contribute to energy dissipation in some tissues.

The relative contribution of these pathways is likely to vary according to species, developmental stage, nutritional status, and environmental temperature. Therefore, UCP1-mediated BAT thermogenesis remains the most established NST mechanism, while several alternative mechanisms continue to be investigated.

Regulation of non-shivering thermogenesis

The sympathetic nervous system plays a central role in initiating the thermogenic response to cold. When body temperature begins to fall, cold-sensitive pathways activate the central thermoregulatory system, resulting in increased sympathetic activity.

Norepinephrine released by sympathetic nerve terminals stimulates thermogenic tissues. In BAT, it promotes lipolysis and UCP1-dependent heat production. In skeletal muscle, sympathetic and metabolic signaling can influence pathways involved in increased energy expenditure and thermogenesis.

Therefore, NST is not an isolated process occurring independently in individual tissues. It forms part of an integrated thermoregulatory response involving the nervous system, endocrine signals, metabolism, and thermogenic tissues.

Importance of Non-Shivering Thermogenesis in Neonates

The importance of NST becomes particularly evident immediately after birth. Neonates can lose heat rapidly through conduction, convection, radiation, and evaporation. If heat loss exceeds the capacity for heat production, body temperature decreases and hypothermia can develop.

Hypothermia can have major consequences because maintaining body temperature requires considerable metabolic energy. Increased thermogenesis can consume glucose, fatty acids, and oxygen, potentially contributing to metabolic stress when energy reserves are limited.

Premature and low-birth-weight neonates are especially vulnerable because their thermoregulatory mechanisms and energy reserves may be less developed. Environmental temperature, nutritional status, oxygen availability and disease can also influence their ability to support thermal balance.

For newborn animals, appropriate environmental management is therefore essential. Providing adequate warmth reduces excessive heat loss and decreases the metabolic

demand placed on the neonate's thermogenic system.

Physiological Significance

NST provides an efficient survival mechanism during exposure to cold. Rather than depending entirely on muscular shivering, the neonate can increase metabolic activity in specialized tissues and generate heat internally.

BAT-mediated thermogenesis is particularly effective because UCP1 directly converts mitochondrial energy into heat. Muscle-based mechanisms provide an additional potential source of heat and may become particularly important when BAT activity is insufficient or when skeletal muscle contributes substantially to whole-body energy expenditure.

The combined activity of BAT, skeletal muscle and other metabolic pathways therefore provides a flexible system for maintaining thermal homeostasis.

Conclusion

Non-shivering thermogenesis is a fundamental component of neonatal thermoregulation. Because newborns have a limited capacity for effective shivering, they depend substantially on metabolic mechanisms to generate heat. Brown adipose tissue and UCP1-mediated mitochondrial uncoupling represent the classical and best-established pathway of NST. However, skeletal muscle can also contribute through mechanisms such as sarcolipin-mediated SERCA uncoupling and increased Ca^{2+} cycling. Creatine cycling, lipid cycling and other forms of mitochondrial energy dissipation may provide additional contributions.

A better understanding of these mechanisms is important for appreciating how neonates adapt to the thermal challenges encountered after birth. It also highlights the importance of appropriate thermal management in preventing neonatal cold stress and hypothermia.

References

- Reece WO, Erickson HH, Goff JP, Uemura EE, editors. Dukes' Physiology of Domestic Animals. 13th ed. Ames, IA: Wiley-Blackwell; 2015.
- Cunningham JG, Klein BG. Cunningham's Textbook of Veterinary Physiology. 6th ed. St. Louis, MO: Elsevier; 2020.
- Guyton AC, Hall JE. Guyton and Hall Textbook of Medical Physiology. 14th ed. Philadelphia, PA: Elsevier; 2021.
- Bal NC, Maurya SK, Sopariwala DH, et al. Sarcolipin is a newly identified regulator of muscle-based thermogenesis in mammals. *Nature Medicine*. 2012;18(10):1575–1579.
- Periasamy M, Maurya SK, Mijares JR, et al. Sarcolipin: a key thermogenic and metabolic regulator in skeletal muscle. *Trends in Endocrinology & Metabolism*. 2017;28(8):554–566.
- Lowell BB, Spiegelman BM. Towards a molecular understanding of adaptive thermogenesis. *Nature*. 2000;404:652–660.
- Kazak L, Chouchani ET, Jedrychowski MP, et al. A creatine-driven substrate cycle enhances energy expenditure and thermogenesis in beige fat. *Cell*. 2015;163(3):643–655.
- Rousset S, Alves-Guerra MC, Mozo J, et al. The biology of mitochondrial uncoupling protein 1 and thermogenesis. *Biochimica et Biophysica Acta (BBA) – Molecular Cell Research*. 2004;1556(1):79–94.

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