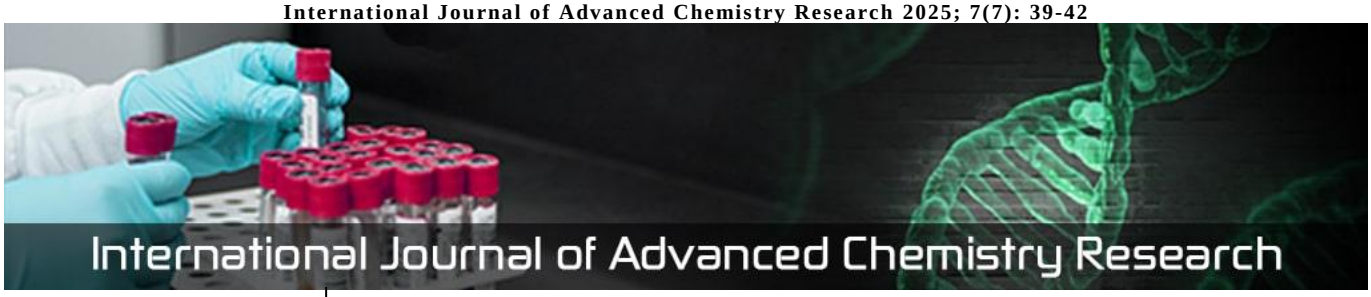

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Noor AL-Huda Salah AL-Zuhairy
Department of Pharmacology and Toxicology, College of Pharmacy, Mustansiriya University, Baghdad, Iraq

Zahraa Ali Mohammed
Assistant Lecture, Department of Clinical Laboratory Sciences, Collage of Pharmacy, Al-Qadisiyah University, Baghdad, Iraq

Huda Sabah Jabr
Department of Pharmacology and Toxicology, College of Biotechnology, University of Al-Qadisiyah, Iraq

Corresponding Author:
Noor AL-Huda Salah AL-Zuhairy
Department of Pharmacology and Toxicology, College of Pharmacy, Mustansiriya University, Baghdad, Iraq

Function of brown adipose tissue in infant and adult

Noor AL-Huda Salah AL-Zuhairy, Zahraa Ali Mohammed and Huda Sabah Jabr

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Abstract
A particular kind of fat known as brown adipose tissue (BAT) is primarily involved in the process of non-shivering thermogenesis, which is the production of heat for the purpose of maintaining a constant body temperature. When it comes to the metabolism of calories, brown adipose tissue (BAT) makes use of uncoupling protein 1 (UCP1) in its mitochondria, in contrast to white adipose tissue (WAT), which serves as a reserve of energy. The dark hue of BAT and its high metabolic activity are both due to the abundance of mitochondria and capillaries that it contains. Although it is most active in newborns, functional BAT is still present in adults, particularly in the supraclavicular and paravertebral areas of the brain. Its existence in healthy people has been established by recent imaging investigations employing PET/CT, especially when the subjects were exposed to chilly situations.

Keywords: Brown adipose tissue (BAT), non-shivering thermogenesis, uncoupling protein 1 (UCP1), mitochondria

Introduction
There are two types of adipose tissue that make up the adipose organ: white adipose tissue, which is often known as white fat, and brown adipose tissue (BAT). [1] BAT may be found almost everywhere in the animal kingdom. Brown fat is composed of two separate cell types, both of which perform roles that are comparable to one another. The first kind will be seen in larger "classic" deposits and will have an embryological origin that is comparable to that of muscle cells. [2] White adipocytes are stimulated by the sympathetic nervous system, which ultimately leads to the impact that is being considered. Adipose tissue that is white in color contains adipocytes that are either beige or brite in color. There is a particularly high concentration of brown adipose tissue (BAT) in newborns and species that are hibernating. [3] The frequency of its occurrence decreases with age in humans; nonetheless, it continues to be present and physiologically active into maturity. This function's principal purpose is to regulate temperature. In addition to the heat that is generated by muscles that are shivering, brown adipose tissue (BAT) also generates heat via a process known as non-shivering thermogenesis. Brown adipocytes, in contrast to white adipocytes, which only contain a single lipid droplet, contain several smaller lipid droplets and a much larger concentration of iron-rich mitochondria. This is one of the factors that contributes to the deeper pigmentation of brown adipose tissue (BAT).[4] When compared to white adipose tissue, brown adipose tissue contains a higher number of capillaries, which makes it easier for the tissue to receive oxygen and nutrients, as well as distribute the heat that is created.

Anatomical location and histology
FDG-PET imaging was used to identify metastatic tumors in adult patients, which led to the identification of BAT in those individuals. These scans, together with the data from human autopsies, have led to the discovery of many BAT depots. Depots of brown adipose tissue may be seen in neonates in a number of different locations, including the interscapular, supraclavicular, suprarenal, pericardial, and para-aortic areas. These depots are located around the pancreas, kidneys, and trachea. [5] These depots gradually take on the appearance of white adipose tissue as the growth process progresses for them.

The mediastinal, supraclavicular, paravertebral, para-aortic, and suprarenal regions are among the depots that are often seen in adult FDG-PET scans from a clinical perspective. There is ongoing debateon whether or not these depots should be classified as "classical" BAT or as beige or brite fat.[6] Two different cell types are referred to as "brown fat" in both academic papers and general media. This designation is based on the cellular morphology and anatomical placement of these two cell types. Both have a large number of mitochondria that are rich in iron and minute lipid droplets, both of which contribute to the dark pigmentation of the cells.

Brown adipose tissue, which is recognized by its highly vascularized deposits, may be found in certain anatomical sites, such as between the scapulae, around the kidneys, in the cervical and supraclavicular regions, and along the spinal column. These places are situated in the body. There are a few minute lipid droplets that are included in this kind, which is the less significant of the two.

When it comes to adipose tissue, the cell type that may be formed as a result of adrenergic stimulation is referred to as "beige fat." Its lighter brown color is due to the increased variety in lipid droplet dimensions as well as the increased ratio of lipid droplets to mitochondria both of which contribute to the color. [16]

Development

The genesis of brown adipocytes, myocytes, chondrocytes, and adipocytes may be traced back to the mesoderm, which is the intermediate layer of the embryo. Both the traditional muscle and brown adipose tissue populations may trace their roots back to the paraxial mesoderm, which is the stem cell population of the mesoderm. The intrinsic potential to activate the promoter of myogenic factor 5 (Myf5) is a characteristic that is unique to myocytes and this particular population of brown adipose tissue. Both of these cells possess this innate ability. There is no evidence that brown adipose tissue that has been produced by adrenergic stimulation and the progenitors of conventional white adipocytes are able to activate the Myf5 promoter. The cells known as pericytes, which are found inside white adipose tissue and surround the blood vessels, have the potential to give birth to both adipocytes and brown adipocytes. [7] Different from this is the existence of the Myf5 protein, which is involved in the development of a number of different tissues. This is an important distinction. Additionally, brown adipocytes that were not cultured with the transcription factor PRDM16 were able to change into myocytes, but myocytes that were grown with the transcription factor PRDM16 were able to transform into brown adipocytes. [8]

Function

The mitochondria of a eukaryotic cell make use of resources in order to produce adenosine triphosphate (ATP), which is the major source of energy. The proton motive force (PMF) is a term that is often used to describe the accumulation of energy that occurs as a result of a proton gradient across the inner mitochondrial membrane during this process. The energy that is gained from the movement of protons between the ATP synthase enzyme and the membrane (which follows the concentration gradient of the protons) is then used in the production of ATP. The process in question is identified as chemiosmosis. Through a mechanism known as proton leak, endotherms are able to save the body's heat by guiding mitochondria to let protons to flow back down the gradient without facilitating the synthesis of ATP. [9] An uncoupling protein is present in the inner membrane, which provides protons with an alternate path for returning to their orbital. After being actively expelled from the mitochondria by means of the electron transport chain, protons are able to return to the mitochondria with the assistance of uncoupling protein 1, also known as thermogenin. During the process of uncoupling oxidative phosphorylation via this alternate pathway for protons, the energy that is contained within the proton motive force is released as heat. All endothermic cells produce heat to a certain extent, particularly when the temperature of the body falls below a threshold that regulates thermal regulation. Although this is the case, brown adipose tissue is highly specialized for thermogenesis that does not include shivering. When compared to usual cells, each cell initially contains a bigger number of mitochondria than the average cell. These mitochondria have a higher concentration of thermogenin in their inner membrane than other mitochondria they include. [10]

Infants

Brown adipose tissue is located on the dorsal side, along the superior portion of the vertebral column, and around the shoulders of newborns, constituting about 5% of their total mass. Premature newborns are particularly vulnerable to the deadly cold, thus preventing hypothermia is crucial. Infants are more vulnerable to cold than adults for a variety of reasons:

- The increased ratio of body volume, which correlates with heat production, to body surface area, which correlates with heat dissipation.
- A deficiency in thermal insulation, such as subcutaneous adipose tissue and fine body hair (notably in premature infants); The head's relatively larger surface area; The absence of muscular development and the inability or reluctance to shiver.
- The inability to relocate from cold environments, air currents, or materials that dissipate heat; The incapacity to utilize alternative methods for warmth, such as donning clothing, drying the skin, or engaging in physical activity; The nervous system's underdevelopment, resulting in inadequate or delayed responses to cold stimuli (e.g., vasoconstriction of blood vessels in and just beneath the skin).

Brown fat produces heat, which gives a baby another way to regulate their body temperature.

Adults

It was previously thought that as children become older, the majority of the mitochondria in brown adipose tissue, which are responsible for the brown pigmentation of the tissue, undergo a reduction. This results in the tissue becoming more similar to white fat in terms of both appearance and physiology. In very rare cases, brown fat continues to expand rather than involuting, which may lead to the development of a tumor known as a hibernoma. Recent research has shown that brown fat, as opposed to white fat, is more closely associated with skeletal muscle. [11] Brown adipose tissue (BAT) is almost exclusively found in the upper chest and neck areas, particularly paravertebrally, in the majority of people, according to study that was

conducted utilizing positron emission tomography scanning. The residual deposits are less noticeable when an adrenergic beta blocker is administered before to the scan. On the other hand, they are more noticeable when the patient is exposed to cold, which enhances tracer absorption and indicates that metabolic activity is increased. It is possible that these results may lead to the development of innovative weight-loss treatments. Brown fat is responsible for burning calories from normal fat. It has been shown that brown fat may be effectively generated in mice by these researchers. [12] According to the findings of a research that was conducted on mice that were defective in APOE, exposure to cold may hasten the formation of atherosclerotic plaque and make it more unstable and unstable. The study mice were kept at a constant low temperature of 4 degrees Celsius for a period of eight weeks, which may have caused stress owing to the abrupt change in temperature rather than a gradual acclimatization to the new environment. For the purpose of determining the effects of ambient temperature reductions of merely 5 to 10 degrees Celsius on adult humans, this might be carried out. Furthermore, a number of recent research have shown that being exposed to cold environment has considerable positive effects on a wide variety of species, including people. Researchers came to the conclusion that "activation of BAT is an effective therapeutic approach to alleviate hyperlipidaemia and protect against atherosclerosis".[26] Additionally, they discovered that activating brown fat may reduce plasma triglyceride and cholesterol levels while also decreasing the progression of diet-induced atherosclerosis. [14] It is before the present increase in health issues connected to excessive accumulation of white fat, it is vital to conduct longitudinal studies that include adults in order to evaluate the amount of benefits and risks associated with the buildup of white fat. The use of β3-adrenoceptor agonists in pharmacological therapies has shown an increase in glucose metabolic activity in brown adipose tissue in animal models and has been documented in reference. [15]

Furthermore, studies have revealed:

- The stimulation of the basal adipose tissue (BAT) improves glucose homeostasis and insulin sensitivity in humans [16], indicating that it may be beneficial for those who have impaired insulin function. Nonetheless, there exists a broader applicability, as research indicates that even marginally elevated blood glucose levels in healthy, non-diabetic individuals correlate with long-term damage to various organs, including the brain, tendons, eyes, and the endothelial/cardiovascular system, alongside increased concentrations of detrimental advanced glycation end products.
- BAT activation has the potential to have a major impact on bone density as well as bone health.
- The activation of brown adipose tissue resulting from exposure to cold causes an increase in adiponectin concentrations; in adult men, even two hours of cold exposure led to a 70% increase in circulating adiponectin levels. [38] It is possible that there is a relationship between longevity and the production of adiponectin, given that studies have shown that both male and female centenarians have greater levels of circulating adiponectin and genetic factors that enhance adiponectin synthesis. [39] In addition, centenarians who had greater levels of plasma adiponectin had improved metabolic indicators, as well as lower levels of C-reactive protein and E-selectin. [18]
- There is a correlation between longer life expectancy and the generation of fibroblast growth factor 21 (FGF-21).[41] The activation of brown adipose tissue (BAT) in humans is triggered by cold exposure, which results in a 37% rise in the amount of circulating fibroblast growth factor 21 (FGF21). Because it improves insulin sensitivity and glucose metabolism, FGF21 may be responsible for some of the aspects that contribute to its longevity-promoting properties.
  As a result of exposure to cold, circulation irisin levels increase.[19] Irisin, which is similar to exercise, has a variety of benefits, including improved insulin sensitivity, increased bone density and quality, the promotion of the formation of lean muscle, and a reduction in obesity via the conversion of white fat to brown fat. In comparison to healthy centenarians, who have larger levels of serum irisin, young persons who have had a myocardial infarction have much lower levels of this protein. Based on these results, more study might be conducted to investigate the function that irisin plays in the regulation of lifespan and vascular illnesses. [20]

Insulin sensitivity and thermogenesis are both increased when brown adipose tissue and skeletal muscle are exposed to cold. This is because cold exposure causes an increase in SIRT1 phosphorylation and activity. Increased levels of SIRT1 have been shown to have a favorable correlation with human lifespan. In conjunction with other sirtuins, SIRT1 is responsible for a variety of metabolic effects; however, its ability to enhance insulin sensitivity, regulate glucose levels in skeletal muscles, drive white adipose tissue to brown, and boost the activity of brown adipose tissue is of utmost importance for improving health and extending longevity.
Altering the gut flora, reducing obesity and metabolic disorders brought on by a high-fat diet, and encouraging the browning of white adipose tissue are all benefits of intermittent fasting, especially when it is done every other day.

Brown fat solves the problem of obesity:

Since obesity rates are high right now, researchers are searching for methods to help people lose weight, such as reducing food consumption or increasing energy expenditure. Exercise is one way to burn energy, but BAT also plays a role in energy consumption. By dispelling energy as heat, it may be able to counterweight gain. Although scientists are still unsure of how humans could boost their brown fat composition, there is some hope that figuring out how to convert more white fat to brown fat could aid in weight loss or stop further weight gain. It is uncertain, nevertheless, whether this is feasible or beneficial.

Conclusion

To enable such treatments, basic understanding of the synthesis of brown fat and the control of its activity is essential. We incorporate the latest findings on how hormonal and developmental cues control the production and activity of brown fat in connection to its metabolic role.

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