Physical exercise as a key to activating fat burning through the activation of uncoupling protein 1 (ucp1) in adipose tissue: a scoping review

El ejercicio físico como clave para activar la quema de grasa a través de la activación de la proteína desacopladora 1 (UCP1) en el tejido adiposo: una revisión del alcance

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Abstract

Background: In addition to being an important element related to thermogenesis, exercise is an excellent intervention to reduce obesity. Recent research indicates that "exerkines," or chemicals released during physical activity, can change the Brown adipose tissue (BAT) activation and white adipose tissue browning. The compound processes by which BAT activation is affected by peripheral variables brought on by exercise, however, are not well understood. Moreover, the impact effect physical activity on BAT activation is not well understood. One important protein in charge of both white and brown adipose tissue exhibit adaptive thermogenesis going through browning is Uncoupling Protein 1 (UCP1). Objective: This study aims to analyze the effect of physical exercise on increasing uncoupling protein 1 (UCP1) in mice.
Materials and methods: We looked through a number of literature databases for our systematic review investigation, including Pubmed, Web of Science, and Science Direct. articles that addressed physical activity and UCP1 that were released within the last five years. The Web of Science, Pubmed, and Science Direct databases were used to locate 380 published articles. For this systematic review, ten papers that met the inclusion criteria were selected and reviewed. Systematic Reviews and Meta-Analyses' Preferred Reporting Items (PRISMA) were used in this study to assess standard operating procedures.
Results: The findings of this study indicate that physical exercise has been shown to increase UCP1 expression.
Conclusions: It has been demonstrated that physical activity increases UCP1 expression. The process of boosting metabolism and thermogenesis will be triggered by this rise. in order for the energy expenditure generated by adipose tissue to increase.

Keywords

Physical exercise; physical fitness; bat; ucp1; fatty acid.

Resumen

Antecedentes: Además de ser un elemento importante relacionado con la termogénesis, el ejercicio es una excelente intervención para reducir la obesidad. Investigaciones recientes indican que las "exerkinas", o sustancias químicas liberadas durante la actividad física, pueden cambiar la activación del tejido adiposo marrón (BAT) y el oscurecimiento del tejido adiposo blanco. Sin embargo, no se comprenden bien los procesos compuestos por los cuales la activación del BAT se ve afectada por las variables periféricas provocadas por el ejercicio. Además, no se comprende bien el efecto del impacto de la actividad física en la activación del BAT. Una proteína importante a cargo de la termogénesis adaptativa que se produce durante el oscurecimiento del tejido adiposo blanco y marrón es la proteína desacopladora 1 (UCP1). Objetivo: Este estudio tiene como objetivo analizar el efecto del ejercicio físico en el aumento de la proteína desacopladora 1 (UCP1) en ratones.
Materiales y métodos: Buscamos en varias bases de datos bibliográficas para nuestra investigación de revisión sistemática, incluidas Pubmed, Web of Science y Science Direct. Artículos que abordaron la actividad física y la UCP1 que se publicaron en los últimos cinco años. Se utilizaron las bases de datos Web of Science, Pubmed y Science Direct para localizar 380 artículos publicados. Para esta revisión sistemática, se seleccionaron y revisaron diez artículos que cumplían los criterios de inclusión. En este estudio se utilizaron los elementos de informe preferidos de revisiones sistemáticas y metaanálisis (PRISMA) para evaluar los procedimientos operativos estándar.
Resultados: Los hallazgos de este estudio indican que se ha demostrado que el ejercicio físico aumenta la expresión de UCP1.
Conclusiones: Se ha demostrado que la actividad física aumenta la expresión de UCP1. El proceso de aumento del metabolismo y la termogénesis se desencadenará por este aumento, para que aumente el gasto energético generado por el tejido adiposo.

Palabras clave

Ejercicio físico; aptitud física; bat; ucp1; ácido graso.

Introduction

Obesity has become a deadly global issue and a serious societal challenge in the healthcare system. Chronic diseases such as obesity are very complex that in the absence of prevention efforts will trigger damage to human tissues and lead to several conditions include diabetes mellitus, heart disease, and malignancies, which can greatly jeopardize the life expectancy of patients and their overall quality of life, besides obesity is also linked to substantial morbidity and mortality, encompassing human chronic diseases and early death (Koliaki et al., 2023). An unhealthy lifestyle that starts with overeating, inactive living style, inactivity, lack of exercise, and lack of mobility will trigger excessive weight gain and lead to obesity (Sugiharto et al., 2021). The energy imbalance triggered by the factors that cause obesity will cause dysfunction in energy formation, which results in the white fat tissue's activation (N. Kim et al., 2018). In addition, the impact that occurs is less than optimal performance of fatty acid metabolism (Flouris et al., 2017).

The lack of fibroblasts and the sparseness of fibrous components define adipose tissue as a connective tissue (Said et al., 2022). Human body fat belongs to the category of loose connective tissue rather than dense connective tissue (De Sanctis et al., 2025). The majority of the cells in adipose tissue are called adipocytes (De Sanctis et al., 2025). The two functional types of adipose tissue are brown adipose tissue (BAT) and white adipose tissue (WAT) (Chou et al., 2024). BAT is indicated by elevated mitochondrial content and uncoupling protein 1 (UCP1) expression. UCP1 has the ability to without chills convert energy into heat through thermogenesis, increasing energy expenditure (Cohen & Kajimura, 2021).

Adopting a healthy lifestyle and regular physical exercise can enhance brown fat tissue activation and fat oxidation metabolism (Sugiharto et al., 2021). Exercise is thought to be a highly effective strategy for preventing and lowering the incidence of overweight and obesity (Rodrigues et al., 2018). This is due to the fact that exercise can stimulate brown fat tissue and raise fat oxidation (Purdom et al., 2018) to more effectively stimulate the production of uncoupling protein-1 (UCP-1) (S. H. Kim & Plutzky, 2016). However, exercise can also raise oxidative stress and change the body's metabolism (Wibawa et al., 2021). Reduced protein expression in the mitochondrial membrane, increased white fat deposits in adipose tissue, and poor fat oxidation can result from this (Huh, 2018). On the other hand, proper intensity training can boost fat metabolism, allowing for the production of brown fat tissue triggered by the hormone irisin (Jabbour & Iancu, 2017).

The increase in fat metabolism that occurs during exercise can also make the body healthier. Exercise is positively connected with several factors, including your body shape, according to numerous research (Said et al., 2022), physical fitness (Said et al., 2021), and cardiometabolic biomarkers (Leskinen et al., 2023). Exercise and other lifestyle changes can increase metabolism, but many of the underlying mechanisms are still unclear. Norepinephrine and β-adrenergic receptors are activated by exercise to trigger beneficial tissue adaptations. This has the ability to prevent obesity and metabolic problems (Vidal & Stanford, 2020). Brown adipocyte lipolysis and mitochondrial respiration are initiated after adrenergic stimulation, which is dependent on UCP1 expression (Ikeda & Yamada, 2020). There is compelling evidence thermogenic fat cells, such as the sympathetic nervous system (SNS) innervates brown and beige adipocytes, which can be triggered by exposure to cold and food (Chou et al., 2024). However, research about whether and how to work out controls thermogenic fat cells yields contradictory findings when contrasted with cold exposure (Garritson & Boudina, 2021). According to some studies, exercise itself does not increase thermogenesis by BAT and is a form of heat generation (Lehnig & Stanford, 2018). BAT is a thermogenic tissue involved in heat production and energy expenditure (Foster & Frydman, 1979). Given that exercise also increases energy expenditure and heat production, it is not surprising that BAT is decreased by exercise to maintain body temperature. So this is still a matter of debate among researchers and needs further exploration.

The production of the releasing protein UCP1, which accelerates electron transport and generates heat, is the best studied mechanism of adipocyte thermogenesis (Desai et al., 2024). Due to its role in non-shivering thermogenesis, releasing protein 1 (UCP1) is found in the inner mitochondrial membrane (Porter, 2017). When UCP1 is activated, it enables large proton conductance in the inner membrane. This unleashes respiration and mitochondrial fuel oxidation of ATP production (Porter, 2017). The substantial negative association between the amount of thermogenic adipose tissue and the risk of metabolic diseases has drawn attention to the need to understand the mechanisms behind the development

and maintenance of UCP1-expressing adipocytes in humans (Becher et al., 2021). Most of the research on how to control thermogenesis is done in mice, where catecholamines released upon exposure to cold increase UCP1 transcription (Collins, 2022). In addition, increased UCP1 expression is also triggered by exercise (Sugiharto et al., 2021). There is still much to learn about the underlying mechanics. The signal transduction steps that lead to an increase in UCP1 during exercise are important to understand in order to demonstrate the thermogenic mechanisms of exercise. As a result, this systematic review will thoroughly examine the cellular mechanisms and effects of physical exercise on the rise in UCP1.

Materials and method

Study Design

Researchers perform a thorough search through journal databases like Science Direct, Web of Science, and Pubmed for this kind of systematic review investigation. These venues are regarded as the best in the world for gathering papers with a significant effect and a solid scientific foundation. This initial search technique eliminates duplicate articles. The search results are further filtered using pre-established inclusion and exclusion criteria.

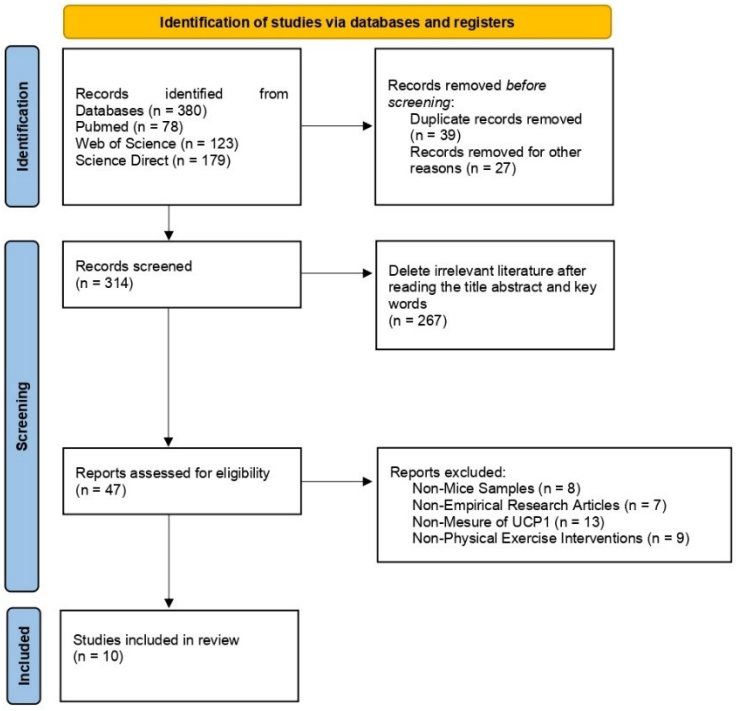
Eligibility Criteria

The inclusion criteria for this study were made by looking at publications from the previous five years that discussed physical activity and UCP1 expression and also involved samples must be mice and no intervention other than physical exercise intervention. So the keywords we used were physical activity and UCP1 expression to find the papers we wanted to search for. In addition, exclusion criteria that were not included in our review analysis were papers that did not comply with scientific validity guidelines or were not listed in reliable search indexes such as Web of Science, Pubmed, or Science Direct. So they were not included in our study, in addition, the criteria if human samples were not included in our analysis.

Procedure

Following verification and review, the publications' full text, abstract, and title were added to the Mendeley database. Using the databases Science Direct, Pubmed, and Web of Science, 380 publications were located in the first phase. Following title suitability screening, 314 papers that satisfied the criteria were chosen for the second screening stage. 47 papers were found in the third stage after the title, abstract, and keywords were read. After reading the entire paper, we made the following decisions based on suitability: the study should be experimental, the intervention should be physical activity, the biomarker should be UCP1 gene expression, and the sample should be mice. We now arranged the products according to their general suitability. Following a rigorous review and observation process, ten papers that satisfied the inclusion criteria were chosen for analysis. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) evaluation served as the operational criterion for this study.

Figure 1. PRISMA flowchart of the article selection process



Results

Table 1. Summary of the design and intervention of the studies

Author	Design	Participants	Participants Age	Intervention	Outcome
(Kianmehr et al., 2020)	Randomized controlled trial	Forty-five adult male Wistar albino rats in good health (Rattus norvegicus)	8 weeks old	1. Mice were introduced to running on a treadmill for 1 week. 2. Animals are exercised on a motorized treadmill running at 9 meters per minute. 3. Exercise was performed per session for 20 minutes. 4. Intervention was done 5x a week for 2 weeks of treatment 5. The rats were trained for 10 minutes daily on the first day of exercise at a speed of 11 m/min. 6. The speed increased gradually until it reached 26 minutes per day in the second week.	1. In the group with exercise intervention, UCP1 expression levels increased significantly.
(Chou et al., 2024)	Randomized controlled trial	Fifty male mice	5 week old	1. All groups had a week of exercise adaptation prior to treatment. 2. For 40 minutes at 0% inclination, the aerobic exercise group was instructed to run on a motorized treadmill at a pace of 15 m/min. 3. Resistance exercise was performed by climbing stairs while holding weights. 4. Rats warmed up on a treadmill without elevation for ten minutes at a speed of five to seven meters per minute for HIIT. After that, they alternated between running for one minute at a pace of 18–20 m/min (about 80% MRS) and two minutes at a pace of 10–12	1. The HIIT group increased UCP1 expression significantly higher than the no exercise intervention group.

				m/min (40–50% MRS) for ten rounds every day.	
(de Melo et al., 2022)	Randomized controlled trial	Swiss mice	8 week old	1. Prior to the exercise intervention, the rats were adapted. 2. There were 20 climbing series in each workout, with 70% workload and 60–90 second rest periods in between sets. 3. The animals received training for five days in a row.	1. There was a significant increase in UCP1 expression after the physical exercise intervention.
(Xiao et al., 2023)	Randomized controlled trial	68 male Sprague Dawley rats	Five week old	1. Exercise adaptation is done for 1 week. 2. After 1 week of adaptive training, the rats in the training group underwent the following training program 5 times a week for 10 weeks: 4 sessions of 1 min of high-intensity exercise (18 m/min) with 10.5 min of interval training (9 m/min) in the first 2 weeks, and 12 sessions of 1 min of high-intensity exercise (30 m/min) with 2.5 min of interval training (18 m/min) in weeks 3 to 10.	1. There was a significant increase in UCP1 expression in the HIIT intervention group.
(Yin et al., 2022)	Randomized controlled trial	24 male mice	6 week old	1. Before training, the adaptation process is carried out first. 2. The exercise group underwent daily physical exercise on the walking wheel system for 1 hour/day, 5 days/week for 8 weeks of intervention. 3. In the first week, the exercise rats started running at a speed of 4 m/min, which was then increased daily by 0.2 m/min and reached 5.2 m/min at the end of the first week on the rat walking wheel system (SANS, China). 4. In the following weeks, the rats ran at a speed of 5.2 m/min for 1 hour/day.	1. There was a significant increase in UCP1 expression in the group with exercise intervention.
(Khalafi et al., 2020)	Randomized controlled trial	Forty male Wistar rats	Seven week old	1. Mice were first subjected to exercise adaptation. 2. Physical exercise intervention was conducted 5x a week for 12 weeks. 3. Running is done on a treadmill. 4. The MICT protocol required constant operation between 65% and 70% of its top speed. 5. From 12 m/min in the first week to 16 m/min in the tenth week, the treadmill speed was gradually increased and then maintained for the last two weeks. 6. Ten 4-minute high-intensity running sessions lasting 85% to 90% of maximal speed were part of the HIIT program, which also included a 2-minute active rest interval at 50% maximal speed. 7. Over the course of ten weeks, the interval speed was progressively raised and held steady for the final two weeks. 8. Consequently, the treadmill speed rose from 17 m/min in week 1 to 26 m/min in week 10.	1. The HIIT and MICT groups had a significant increase in UCP1 expression than the control group.
(Takaishi et al., 2021)	Randomized controlled trial	33 male rats	Four week old	1. The training group of rats spent 12 hours a day, from 20:00 to 8:00, in individual cages with freely accessible running wheels. 2. Mice could use the running wheel to run whenever they wanted.	1. There was a significant increase in UCP1 expression in the group with physical exercise intervention.

				3. Running distance and time over a 12-hour period were used to capture voluntary running.	
(de Carvalho Picoli et al., 2020)	Randomized controlled trial	Thirty Swiss male mice	45 days old	1. The rats spent three days in a row becoming used to the treadmill prior to exercise. 2. Thereafter, the rats underwent an additional test to determine the peak speed customized for the rat, repeated weekly to adjust the exercise load. 3. Aerobic exercise lasted for 8 weeks, at 70% intensity. 4. 4. With a 0° slope, sessions lasted 30 to 40 minutes in week one, 35 to 50 minutes in week two, 50 to 60 minutes in week three, and 60 minutes in weeks four through eight. 5. Total training 5 sessions a week for a total of 40 training sessions. 6. Rats in the endurance training group experienced stair climbing for three days in a row. 7. The training load was readjusted based on the maximal weight lifted during the incremental test following the adaptation period. 8. The eight-week workout regimen included four series of climbing that were based on 50%, 75%, 90%, and 100% overload, allowing for eight to twelve dynamic movements (repetitions).	1. There was a significant increase in UCP1 expression in the group with physical exercise intervention both resistance training and aerobic exercise.
(Guo et al., 2023)	Randomized controlled trial	Male mice	4 week old	1. Before the physical exercise intervention, all rats in the exercise group were adapted for 1 week. 2. Rats were trained to swim for 60 minutes every day, five days a week, for eight weeks without any physical activity starting in the second week. 3. In endurance training, rats used weights to climb stairs. 4. Up until the eighth week of the intervention, the load was progressively raised. 5. An animal treadmill was used for aerobic exercise.. 6. The exercise began at 8 m/min for 10 minutes on the first day and was increased to 15 m/min for 60 minutes on the fifth day. 7. The pace was kept at 15 m/min and running for 60 minutes, five days a week, for eight weeks starting in the second week. 8. For eight weeks, HIIT exercise was conducted five times a week on a treadmill with a 25° slope. 9. The rats began the 8-week training with a 10-minute warm-up at a speed of 5 m/min. HIIT comprised 10 sessions of 4 min high-intensity treadmill running, separated by 2 min total rest. 10. Over the course of eight weeks, the HIIT speed increased steadily from 16 to 26 m/min.	1. Aerobic training and HIIT groups were shown to significantly increase UPC1 expression.
(H. J. Kim et al., 2022)	Randomized controlled trial	Male mice	8 week old	1. As an aerbic exercise, mice voluntarily ran on wheels.	1. The exercise group had significantly higher UCP1 expression than the control group.

	2. The exercise group performed this activity daily for four weeks. 3. Daily running lengths were tracked using an activity wheel running counter (STARRLife Science, PA, USA)..

Discussion

This study's objective was to determine how exercise can increase the expression of UCP1. Based on the results of a systematic review that has been analyzed, it proves that engaging in physical activity can boost UCP1 expression. Other research results are shown by Kianmehr et al., 2020 proved that mice that have been given aerobic traning interventions performed Five times a week for 20 minutes each session and carried out for two weeks proved to significantly $p<0.05$ can increase UCP1 expression. The findings of additional research also demonstrate that mice that have been given resistance training interventions weight training with climbing done using stairs and carried out for 5 consecutive days proved to significantly $p<0.05$ increase UCP1 (de Melo et al., 2022). Similarly, research has shown that HIIT exercise can significantly increase UCP1 expression (Chou et al., 2024). Thus, exercise has been shown to significantly increase UCP1 expression.

The results of another study proved that HIIT training performed 4 sessions a week for 10 weeks in rats was shown to significantly increase UCP1 expression $p<0.05$ (Xiao et al., 2023). Research results from Yin et al., 2022 that physical exercise performed 5x a week for 8 weeks of intervention given to mice proved significant $p<0.05$ can increase UCP1 expression. Both the intervention of both high-intensity interval training and moderate-intensity continuous exercise are crucial for raising UCP1 in mice (Khalafi et al., 2020). Furthermore, aerobic exercise and resistance training that have been given to mice for 8 weeks significantly $p<0.05$ proved to increase UCP1 expression (de Carvalho Picoli et al., 2020). There is also an increase in UCP1 in mice after physical exercise from the study by (Takaishi et al., 2021).

Another study found that eight weeks of HIIT led to more positive adaptations in cardiometabolic health in overweight/obese individuals compared to MICT. Most of the positive effects of the HIIT protocol were also found to be longer lasting and maintained after cessation of high-intensity interval running for 4 weeks (Gripp et al., 2021). This could be indicated by higher UCP1 expression levels in HIIT training than MICT training. However, further research is needed to confirm this.

Thus, physical exercise was shown to significantly increase fat burning through the expression of UCP1, which is key in activating burning in adipose tissue. However, more details must be discussed regarding the underlying mechanism. Here we discuss in depth the response and physiological mechanism of physical exercise to increase UCP1 expression.

Overview of UCP1 Gene Expression

Uncoupling protein, also referred to as UCP, is an important transmembrane protein present within the mitochondrial membrane. UCP is also a member of the mitochondrial anionic transporter family (Ramsden et al., 2012). UCPs perform and contribute to many things, from oxidative phosphorylation to thermogenesis (dissipating energy through heat), and are crucial in controlling the potential of the mitochondrial membrane (Liu et al., 2006). The molecular mass of these proteins usually ranges from 31 to 34 kDa. The five UCP isoforms, which range from UCP1 to UCP5, are also found in a variety of taxa and tissues, including fungi, plants, mammals, and protozoa (Klingenberg et al., 1999). Up to 10% of the mitochondrial protein is found in brown adipose tissue (BAT), where UCP1 is mostly expressed (Ko et al., 2014). UCP1 is expressed in white adipose tissue (WAT) in addition to brown adipose (Okamatsu-Ogura et al., 2013).

In the majority of cell types, cellular respiration and ATP generation are interconnected processes that don't happen independently. However, proton conductance, which is mediated by a fatty acid/H+ import pathway, determines BAT's ability to produce heat. Release protein 1 (UCP1), which is only expressed in this tissue, mediates this process (Fedorenko et al., 2012). Physical activity, necessary energy

expenditure (needed to perform cellular processes), and adaptive thermogenesis are some of the primary components of energy expenditure. We call this final procedure adaptive energy dissipation. It mostly happens in beige and brown adipocytes in response to eating too much or changing the temperature (Roesler & Kazak, 2020).

BAT activation boosts fatty acid oxidation and glucose absorption, which enhances the body's energy production (Bartelt et al., 2011). The expression of the BAT-specific protein coupling release protein 1 (UCP1) is crucial for BAT's thermogenic function (Wang & Seale, 2016). UCP1 uncouples oxidative phosphorylation from ATP production and transfers protons that are located in the mitochondrial membrane. This releases energy as heat, allowing protons to leave the mitochondria (Fedorenko et al., 2012). During cold acclimatization, mice lacking UCP1 exhibit intolerance to cold and rely on thermogenesis, or shivering, to keep their bodies warm (Golozoubova et al., 2001). Moreover, mice deficient in UCP1 were fat in thermoneutral (30 °C) environments (Feldmann et al., 2009). Prior research has demonstrated that UCP1-deficient animals have aberrant mitochondrial crest architecture and a decreased quantity of electron transport chain components in cold-induced BAT (Kazak et al., 2017).

Significant insight into the mechanisms underlying BAT thermogenesis can be gained by comprehending the molecular mechanisms governing UCP1 expression. In BAT, UCP1-mediated non-shivering thermogenesis is crucial for maintaining energy balance and controlling body weight in both humans and rodents (Chouchani et al., 2019). Treatment for obesity and other metabolic disorders may focus on UCP1-activated thermogenesis (Su et al., 2025). Therefore, it is imperative to find functional enhancers that regulate UCP1 expression and elucidate how chromatin circles regulate UCP1 expression. Knowing the molecular mechanisms responsible for the transcriptional regulation of UCP1 may offer new goals to address obesity and other metabolic disorders. The sympathetic nervous system allows brown adipocytes to perform metabolic activities in response to cold-induced norepinephrine release. There, they use the energy stored in lipids and carbohydrates to generate heat. One important mechanism for boosting energy expenditure and heat generation is UCP1, whose overexpression is linked to weight loss and heightened cold sensitivity (Kozak & Anunciado-Koza, 2008).

Mechanisms by which Physical Exercise Increases UCP1 Gene Expression

Type 2 diabetes, obesity, and additional metabolic conditions are examples of chronic illnesses that can be prevented through non-drug approaches such as exercising regularly (Dewal & Stanford, 2019). A healthy lifestyle with frequent exercise ought to be mandatory in order to avoid chronic diseases from occurring (Müller et al., 2016). In addition, exercising regularly can control bodily processes and energy balance (Garneau et al., 2020). Significant reductions in early demise and chronic disease can be achieved through regular exercise (Leal et al., 2018). Previous studies found that exercise increases UCP1. In essence, UCP1 activation in white and brown fat cells can be triggered by stimuli like cold, exercise, and medications. This activation can enhance circumstances like obesity and promote heat production. The location and mass of WAT and BAT fat in both healthy and obese individuals are stimuli that impact UCP1 expression (Gong et al., 2024). The ability of brown or brite adipocytes to thermogenically respond requires UCP1 activation (Kajimura et al., 2015).

UCP1 plays a significant part in the heat production of beige adipocytes and classical BAT, but due to an intrinsic inhibitory mechanism, UCP1 does not secrete heat at all (Li & Fromme, 2022). One way to increase BAT heat consumption is by activating UCP1. During exercise, a number of metabolites such as succinate, acetate, creatine, and FFA are produced which affect fat thermogenesis and browning. Vigorous exercise increases lipolysis, releases FFA bound to UCP1, and directly increases thermogenesis (Fedorenko et al., 2012). FFAs also activate the nuclear receptor HNF4alpha. The liver then produces acylcarnitine, which helps brown fat thermogenesis occur (Simcox et al., 2017). Creatine metabolism in muscle and adipose tissue creates more creatine, which in turn generates mitochondrial ATP and creatine, which in turn produces ADP and PCr in a 1:1 stoichiometry. Since ATP is heavily used to generate energy during acute exercise, the PCr pool promotes ADP phosphorylation at the substrate level to produce ATP (Zhu et al., 2022). There is proof that the metabolism of arginine and creatine is what causes the cream-colored adipose marks (Kazak et al., 2015).

The electron transport chain produces a proton gradient that is eliminated by UCP1 when activated (Chouchani et al., 2019). Exercise-induced increased activation of peripheral proliferator-activated receptor 1-alpha (PGC-1α) gene in human skeletal muscle promotes the development of UCP-1 (Reisi et

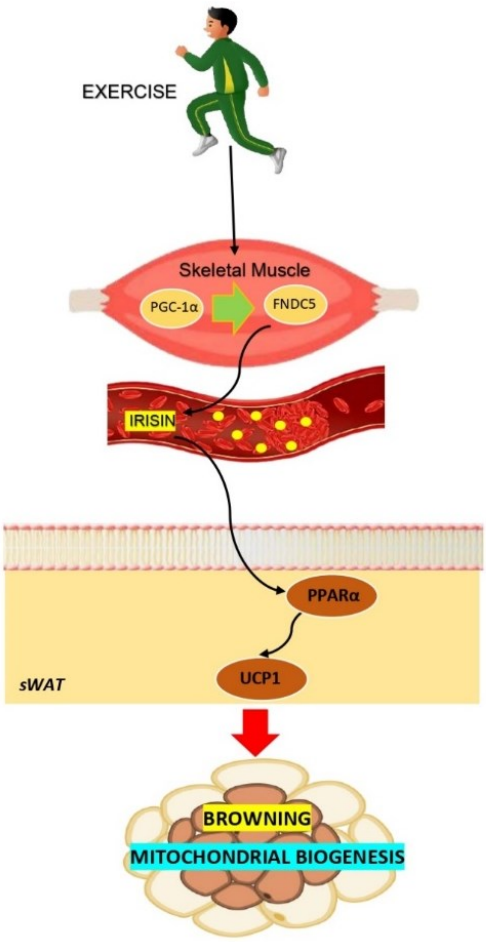
al., 2016). PGC-1α increases a protein with five fibronectin type III domain 5 (FNDC5) that is split and released into the bloodstream as irisin. On the other hand, PGC-1α drives various complex gene regulatory networks that regulate transcription, which are involved in the control of mitochondrial tissue content resulting in the production of brown adipose tissue (BAT) (Dinas et al., 2017). Muscle contraction and sympathetic nerve stimulation are impacted by exercise intensity (Aldiss et al., 2018). Stronger muscles during exercise result in improved metabolism, which encourages the growth of PGC-1α; this happens at high intensity as opposed to moderate intensity (Shirvani & Arabzadeh, 2020). PGC-1α regulates oxidative metabolism and mitochondrial biogenesis, including cell type, which increases the production of UCP-1 (Dinas et al., 2017), in both short-term and long-term exercise (Gorski et al., 2018). Physical activity, which is triggered by the PGC-1α co-activator, raises FNDC5 in muscle, which causes irisin to be released, which raises thermogenesis gene stimulants in adipocytes. Additionally, irisin controls the signaling of energy secretion from muscle, which interacts directly with adipose tissue and results in browning. This raises the metabolic profile of white adipose tissue (WAT) and increases the generation of (Qiu et al., 2018).

In addition, brown adipose tissue serves as a metabolically active tissue that contributes to thermogenesis through activating UCP-1, while adipose tissue remains active for energy metabolism (Khalafi et al., 2020). In contrast, the hypothalamus is responsible for thermogenetic processes. Therefore, thermosensory reactions are triggered in the dorsomedial hypothalamus when body temperature changes. Thus, the hypothalamus controls adaptive thermogenesis through this process (Morrison, 2016). A study of rats exposed to cold found that sympathetic nerve activity increased as a result of dorsomedial hypothalamus (DMH) stimulation via thermos sensory input through the median preoptic (Fuller-Jackson & Henry, 2018).

Increased catecholamine secretion during high-intensity exercise may have an impact on elevated UCP-1 expression (Sanchez-Delgado et al., 2015). Adrenergic receptors cause lipolysis and UCP-1 production, activate protein kinase A, and increase catecholamine secretion after raising cyclic adenosine monophosphate (Rodrigues et al., 2018). Noradrenaline binds to adrenergic receptors 3, 1, and 2. Noradrenaline increases the production of signals that interfere with lipolysis, thermogenesis, and gene expression. UCP-1, an unrelated protein in mitochondria that is in charge of proton translocation across the heat-generating respiratory chain, is thereby activated by prolonged beta-adrenergic stimulation from BAT. Furthermore, prolonged BAT adrenergic stimulation causes signals to be produced that raise metabolic rate (De Queiroz et al., 2012) and lessen ROS (reactive oxygen species). (Brondani et al., 2012).

Compared to moderate-intensity exercise, stronger skeletal muscle structures increase UCP-1 levels in high-intensity activities (Huh, 2018). The intensity of muscle construction has an impact on increasing energy demand, oxygen uptake, increasing AMPK and active PGC-1α, and increasing thermogenesis (Khalafi et al., 2020). Thermogenic enhancement caused by expansion of mitochondrial content and UCP-1 expression in white adipose tissue (WAT) due to irisin release (Mai et al., 2020). Energy expenditure also triggers upregulation of muscle PGC-1α transcription, UCP-1 expression, increased heat production, increased iron release, increased protein-membrane FNDC5, and biogenesis in mitochondria (Moienneia & Attarzadeh Hosseini, 2016). Even without a significant increase in temperature, the energy expenditure profile of high-intensity exercise is broader than that of moderate-intensity exercise (Sugiharto et al., 2019). Physical exercise is the best therapy in increasing UPC1 expression, especially in obese patients. So it is highly recommended to do physical exercise regularly. In this systematic review there are still limitations in the discussion only focusing on the paper on physical exercise on increasing UCP1 expression. However, in the future, further research is needed that discusses specific types of exercise such as the interaction between diet, exercise, and UCP1 expression in humans or research that explores how various types of exercise affect thermogenesis in humans specifically is needed to improve the understanding of the mechanisms related to exercise and UCP1.

Figure 2. Physical exercise mechanism increases UCP1 expression



Strenght and Limitations

The advantage of this systematic review is that it only looked at randomized controlled trials, which is the most reliable type of scientific evidence as there is no possibility of an ambiguous causal relationship. In addition, the samples taken were focused on rats that were given physical exercise interventions so that all samples could show homogeneous data and not be mixed with other categories such as human or other animal samples.

The limitation that we encountered was the lack of discussion and discussion related to how physical exercise in increasing UCP1 expression through physiological review and how the mechanism underlying the increase in UCP1 expression. Therefore, this study is considered important to do in order to add insight and repertoire of knowledge related to how the effect of physical exercise in increasing UCP1 expression and how the underlying mechanism theoretically and scientifically so that the results of the study can be a recommendation to always do physical exercise regularly.

Conclusions

Based on the related articles we found, it can be said that regular physical exercise has been shown to increase UCP1 expression. Thus increasing mitochondrial biogenesis which will trigger increased energy production.

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References

Aldiss, P., Betts, J., Sale, C., Pope, M., Budge, H., & Symonds, M. E. (2018). Exercise-induced 'browning' of adipose tissues. *Metabolism: Clinical and Experimental*, *81*, 63–70. https://doi.org/10.1016/j.metabol.2017.11.009

Bartelt, A., Bruns, O. T., Reimer, R., Hohenberg, H., Ittrich, H., Peldschus, K., Kaul, M. G., Tromsdorf, U. I., Weller, H., Waurisch, C., Eychmüller, A., Gordts, P. L. S. M., Rinninger, F., Bruegelmann, K., Freund, B., Nielsen, P., Merkel, M., & Heeren, J. (2011). Brown adipose tissue activity controls triglyceride clearance. *Nature Medicine*, *17*(2), 200–206. https://doi.org/10.1038/nm.2297

Becher, T., Palanisamy, S., Kramer, D. J., Eljalby, M., Marx, S. J., Wibmer, A. G., Butler, S. D., Jiang, C. S., Vaughan, R., Schöder, H., Mark, A., & Cohen, P. (2021). Brown adipose tissue is associated with cardiometabolic health. *Nature Medicine*, *27*(1), 58–65. https://doi.org/10.1038/s41591-020-1126-7

Brondani, L. de A., Assmann, T. S., Duarte, G. C. K., Gross, J. L., Canani, L. H., & Crispim, D. (2012). The role of the uncoupling protein 1 (UCP1) on the development of obesity and type 2 diabetes mellitus. *Arquivos Brasileiros de Endocrinologia & Metabologia*, *56*(4), 215–225. https://doi.org/10.1590/s0004-27302012000400001

Chou, T. J., Lin, L. Y., Lu, C. W., Hsu, Y. J., Huang, C. C., & Huang, K. C. (2024). Effects of aerobic, resistance, and high-intensity interval training on thermogenic gene expression in white adipose tissue in high fat diet induced obese mice. *Obesity Research and Clinical Practice*, *18*(1), 64–72. https://doi.org/10.1016/j.orcp.2024.01.003

Chouchani, E. T., Kazak, L., & Spiegelman, B. M. (2019). New Advances in Adaptive Thermogenesis: UCP1 and Beyond. *Cell Metabolism*, *29*(1), 27–37. https://doi.org/10.1016/j.cmet.2018.11.002

Cohen, P., & Kajimura, S. (2021). The cellular and functional complexity of thermogenic fat. *Nature Reviews Molecular Cell Biology*, *22*(6), 393–409. https://doi.org/10.1038/s41580-021-00350-0

Collins, S. (2022). Adrenergic Receptors and Adipose Tissue Metabolism: Evolution of an Old Story. *Annual Review of Physiology*, *84*, 1–16. https://doi.org/10.1146/annurev-physiol-060721-092939

de Carvalho Picoli, C., Gilio, G. R., Henriques, F., Leal, L. G., Besson, J. C., Lopes, M. A., de Moraes, S. M. F., Hernandes, L., Batista, M. L., & Peres, S. B. (2020). Resistance exercise training induces subcutaneous and visceral adipose tissue browning in Swiss mice. *Journal of Applied Physiology*, *129*(1), 66–74. https://doi.org/10.1152/japplphysiol.00742.2019

de Melo, D. G., Anaruma, C. P., da Cruz Rodrigues, K. C., Pereira, R. M., de Campos, T. D. P., Canciglieri, R. S., Ramos, C. O., Cintra, D. E., Ropelle, E. R., da Silva, A. S. R., Pauli, J. R., & de Moura, L. P. (2022). Strength training alters the tissue fatty acids profile and slightly improves the thermogenic pathway in the adipose tissue of obese mice. *Scientific Reports*, *12*(1), 1–14. https://doi.org/10.1038/s41598-022-10688-w

De Queiroz, K. B., Rodovalho, G. V., Guimarães, J. B., De Lima, D. C., Coimbra, C. C., Evangelista, E. A., & Guerra-Sá, R. (2012). Endurance training blocks uncoupling protein 1 up-regulation in brown adipose tissue while increasing uncoupling protein 3 in the muscle tissue of rats fed with a high-sugar diet. *Nutrition Research*, *32*(9), 709–717. https://doi.org/10.1016/j.nutres.2012.06.020

De Sanctis, J. B., Balda Noria, G., & García, A. H. (2025). Exploring How Adipose Tissue, Obesity, and Gender Influence the Immune Response to Vaccines: A Comprehensive Narrative Review. *International Journal of Molecular Sciences*, *26*(2), 1–31. https://doi.org/10.3390/ijms26020862

Desai, A., Loureiro, Z. Y., Desouza, T., Yang, Q., & Solivan-rivera, J. (2024). cAMP driven UCP1 induction in human adipocytes requires ATGL-catalyzed lipolysis. *Molecular Metabolism*, *90*(October), 102051. https://doi.org/10.1016/j.molmet.2024.102051

Dewal, R. S., & Stanford, K. I. (2019). Effects of exercise on brown and beige adipocytes. *Biochimica et Biophysica Acta - Molecular and Cell Biology of Lipids*, *1864*(1), 71–78. https://doi.org/10.1016/j.bbalip.2018.04.013

Dinas, P. C., Lahart, I. M., Timmons, J. A., Svensson, P.-A., Koutedakis, Y., Flouris, A. D., & Metsios, G. S. (2017). Effects of physical activity on the link between PGC-1a and FNDC5 in muscle, circulating Irisin and UCP1 of white adipocytes in humans: A systematic review. *F1000Research*, *6*(May), 286. https://doi.org/10.12688/f1000research.11107.1

Fedorenko, A., Lishko, P. V., & Kirichok, Y. (2012). Mechanism of fatty-acid-dependent UCP1 uncoupling in brown fat mitochondria. *Cell*, *151*(2), 400–413. https://doi.org/10.1016/j.cell.2012.09.010

Feldmann, H. M., Golozoubova, V., Cannon, B., & Nedergaard, J. (2009). UCP1 Ablation Induces Obesity and Abolishes Diet-Induced Thermogenesis in Mice Exempt from Thermal Stress by Living at Thermoneutrality. *Cell Metabolism*, *9*(2), 203–209. https://doi.org/10.1016/j.cmet.2008.12.014

Flouris, A. D., Dinas, P. C., Valente, A., Andrade, C. M. B., Kawashita, N. H., & Sakellariou, P. (2017). Exercise-induced effects on UCP1 expression in classical brown adipose tissue: A systematic review. *Hormone Molecular Biology and Clinical Investigation*, *31*(2), 1–13. https://doi.org/10.1515/hmbci-2016-0048

Foster, D. O., & Frydman, M. L. (1979). Tissue distribution of cold-induced thermogenesis in conscious warm- or cold-acclimated rats reevaluated from changes in tissue blood flow: The dominant role of brown adipose tissue in the replacement of shivering by nonshivering thermogenesis. *Canadian Journal of Physiology and Pharmacology*, *57*(3), 257–270. https://doi.org/10.1139/y79-039

Fuller-Jackson, J. P., & Henry, B. A. (2018). Adipose and skeletal muscle thermogenesis: Studies from large animals. *Journal of Endocrinology*, *237*(3), R99–R115. https://doi.org/10.1530/JOE-18-0090

Garneau, L., Parsons, S. A., Smith, S. R., Mulvihill, E. E., Sparks, L. M., & Aguer, C. (2020). Plasma Myokine Concentrations After Acute Exercise in Non-obese and Obese Sedentary Women. *Frontiers in Physiology*, *11*(February), 1–8. https://doi.org/10.3389/fphys.2020.00018

Garritson, J. D., & Boudina, S. (2021). The Effects of Exercise on White and Brown Adipose Tissue Cellularity, Metabolic Activity and Remodeling. *Frontiers in Physiology*, *12*(November), 1–7. https://doi.org/10.3389/fphys.2021.772894

Golozoubova, V., Hohtola, E., Matthias, A., Jacobsson, A., Cannon, B., & Nedergaard, J. (2001). Only UCP1 can mediate adaptive nonshivering thermogenesis in the cold. *The FASEB Journal*, *15*(11), 2048–2050. https://doi.org/10.1096/fj.00-0536fje

Gong, D., Lei, J., He, X., Hao, J., Zhang, F., Huang, X., Gu, W., Yang, X., & Yu, J. (2024). Keys to the switch of fat burning: stimuli that trigger the uncoupling protein 1 (UCP1) activation in adipose tissue. *Lipids in Health and Disease* , *23*(1). https://doi.org/10.1186/s12944-024-02300-z

Gorski, T., Mathes, S., & Krützfeldt, J. (2018). Uncoupling protein 1 expression in adipocytes derived from skeletal muscle fibro/adipogenic progenitors is under genetic and hormonal control. *Journal of Cachexia, Sarcopenia and Muscle*, *9*(2), 384–399. https://doi.org/10.1002/jcsm.12277

Gripp, F., Nava, R. C., Cassilhas, R. C., Esteves, E. A., Magalhães, C. O. D., Dias-Peixoto, M. F., de Castro Magalhães, F., & Amorim, F. T. (2021). HIIT is superior than MICT on cardiometabolic health during training and detraining. *European Journal of Applied Physiology*, *121*(1), 159–172. https://doi.org/10.1007/s00421-020-04502-6

Guo, Y., Zhang, Q., Zheng, L., Shou, J., Zhuang, S., Xiao, W., & Chen, P. (2023). Depot-specific adaption of adipose tissue for different exercise approaches in high-fat diet/streptozocin-induced diabetic mice. *Frontiers in Physiology*, *14*(July), 1–13. https://doi.org/10.3389/fphys.2023.1189528

Huh, J. Y. (2018). The role of exercise-induced myokines in regulating metabolism. *Archives of Pharmacal Research*, *41*(1), 14–29. https://doi.org/10.1007/s12272-017-0994-y

Ikeda, K., & Yamada, T. (2020). UCP1 Dependent and Independent Thermogenesis in Brown and Beige Adipocytes. *Frontiers in Endocrinology*, *11*(July), 1–6. https://doi.org/10.3389/fendo.2020.00498

Jabbour, G., & Iancu, H. D. (2017). High-intensity exercise training does not influence body weight but improves lipid oxidation in obese adults: A 6-week RCT. *BMJ Open Sport and Exercise Medicine*, *3*(1), 3–10. https://doi.org/10.1136/bmjsem-2017-000283

Kajimura, S., Spiegelman, B. M., & Seale, P. (2015). Brown and beige fat: Physiological roles beyond heat generation. *Cell Metabolism*, *22*(4), 546–559. https://doi.org/10.1016/j.cmet.2015.09.007

Kazak, L., Chouchani, E. T., Jedrychowski, M. P., Erickson, B. K., Shinoda, K., Cohen, P., Vetrivelan, R., Lu, G. Z., Laznik-Bogoslavski, D., Hasenfuss, S. C., Kajimura, S., Gygi, S. P., & Spiegelman, B. M. (2015).

A Creatine-Driven Substrate Cycle Enhances Energy Expenditure and Thermogenesis in Beige Fat. *Cell*, *163*(3), 643–655. https://doi.org/10.1016/j.cell.2015.09.035

Kazak, L., Chouchani, E. T., Stavrovskaya, I. G., Lu, G. Z., Jedrychowski, M. P., Egan, D. F., Kumari, M., Kong, X., Erickson, B. K., Szpyt, J., Rosen, E. D., Murphy, M. P., Kristal, B. S., Gygi, S. P., & Spiegelman, B. M. (2017). UCP1 deficiency causes brown fat respiratory chain depletion and sensitizes mitochondria to calcium overload-induced dysfunction. *Proceedings of the National Academy of Sciences of the United States of America*, *114*(30), 7981–7986. https://doi.org/10.1073/pnas.1705406114

Khalafi, M., Mohebbi, H., Symonds, M. E., Karimi, P., Akbari, A., Tabari, E., Faridnia, M., & Moghaddami, K. (2020). The impact of moderate-intensity continuous or high-intensity interval training on adipogenesis and browning of subcutaneous adipose tissue in obese male rats. *Nutrients*, *12*(4). https://doi.org/10.3390/nu12040925

Kianmehr, P., Azarbayjani, M. A., Peeri, M., & Farzanegi, P. (2020). Synergic effects of exercise training and octopamine on peroxisome proliferator-activated receptor-gamma coactivator -1a and uncoupling protein 1 mRNA in heart tissue of rat treated with deep frying oil. *Biochemistry and Biophysics Reports*, *22*(October 2019), 100735. https://doi.org/10.1016/j.bbrep.2020.100735

Kim, H. J., Kim, Y. J., & Seong, J. K. (2022). AMP-activated protein kinase activation in skeletal muscle modulates exercise-induced uncoupled protein 1 expression in brown adipocyte in mouse model. *Journal of Physiology*, *600*(10), 2359–2376. https://doi.org/10.1113/JP282999

Kim, N., Kim, J., Yoo, C., Lim, K., Akimoto, T., & Park, J. (2018). Effect of acute mid-intensity treadmill exercise on the androgen hormone level and uncoupling protein-1 expression in brown fat tissue of mouse. *Journal of Exercise Nutrition & Biochemistry*, *22*(1), 15–21. https://doi.org/10.20463/jenb.2018.0003

Kim, S. H., & Plutzky, J. (2016). Brown fat and browning for the treatment of obesity and related metabolic disorders. *Diabetes and Metabolism Journal*, *40*(1), 12–21. https://doi.org/10.4093/dmj.2016.40.1.12

Klingenberg, M., Echtay, K. S., Bienengraeber, M., Winkler, E., & Huang, S. G. (1999). Structure–Function Relationship in UCP1. *International Journal of Obesity*, *23*(October 2014), S24–S29. https://doi.org/10.1038/sj.ijo.0800939

Ko, E. Y., Sabanegh, E. S., & Agarwal, A. (2014). Male infertility testing: Reactive oxygen species and antioxidant capacity. *Fertility and Sterility*, *102*(6), 1518–1527. https://doi.org/10.1016/j.fertnstert.2014.10.020

Koliaki, C., Dalamaga, M., & Liatis, S. (2023). Update on the Obesity Epidemic: After the Sudden Rise, Is the Upward Trajectory Beginning to Flatten? *Current Obesity Reports*, *12*(4), 514–527. https://doi.org/10.1007/s13679-023-00527-y

Kozak, L. P., & Anunciado-Koza, R. (2008). UCP1: Its involvement and utility in obesity. *International Journal of Obesity*, *32*, S32–S38. https://doi.org/10.1038/ijo.2008.236

Leal, L. G., Lopes, M. A., & Batista, M. L. (2018). Physical exercise-induced myokines and muscle-adipose tissue crosstalk: A review of current knowledge and the implications for health and metabolic diseases. *Frontiers in Physiology*, *9*(SEP), 1–17. https://doi.org/10.3389/fphys.2018.01307

Lehnig, A. C., & Stanford, K. I. (2018). Exercise-induced adaptations to white and brown adipose tissue. *Journal of Experimental Biology*, *121*. https://doi.org/10.1242/jeb.161570

Leskinen, T., Lima Passos, V., Dagnelie, P. C., Savelberg, H. H. C. M., De Galan, B. E., Eussen, S. J. P. M., Stehouwer, C. D. A., Stenholm, S., & Koster, A. (2023). Daily Physical Activity Patterns and Their Associations with Cardiometabolic Biomarkers: The Maastricht Study. *Medicine and Science in Sports and Exercise*, *55*(5), 837–846. https://doi.org/10.1249/MSS.0000000000003108

Li, Y., & Fromme, T. (2022). Uncoupling Protein 1 Does Not Produce Heat without Activation. *International Journal of Molecular Sciences*, *23*(5). https://doi.org/10.3390/ijms23052406

Liu, D., Chan, S. L., De Souza-Pinto, N. C., Slevin, J. R., Wersto, R. P., Zhan, M., Mustafa, K., De Cabo, R., & Mattson, M. P. (2006). Mitochondrial UCP4 mediates an adaptive shift in energy metabolism and increases the resistance of neurons to metabolic and oxidative stress. *NeuroMolecular Medicine*, *8*(3), 389–413. https://doi.org/10.1385/NMM:8:3:389

Mai, S., Grugni, G., Mele, C., Vietti, R., Vigna, L., Sartorio, A., Aimaretti, G., Scacchi, M., & Marzullo, P. (2020). Irisin levels in genetic and essential obesity: clues for a potential dual role. *Scientific Reports*, *10*(1), 1–9. https://doi.org/10.1038/s41598-020-57855-5

Moienneia, N., & Attarzadeh Hosseini, S. R. (2016). Acute and chronic responses of metabolic myokine to different intensities of exercise in sedentary young women. *Obesity Medicine*, *1*, 15–20. https://doi.org/10.1016/j.obmed.2015.12.002

Morrison, S. F. (2016). Central control of body temperature. *F1000Research*, *5*(May), 1–10. https://doi.org/10.12688/F1000RESEARCH.7958.1

Müller, M. J., Enderle, J., & Bosy-Westphal, A. (2016). Changes in Energy Expenditure with Weight Gain and Weight Loss in Humans. *Current Obesity Reports*, *5*(4), 413–423. https://doi.org/10.1007/s13679-016-0237-4

Okamatsu-Ogura, Y., Fukano, K., Tsubota, A., Uozumi, A., Terao, A., Kimura, K., & Saito, M. (2013). Thermogenic ability of uncoupling protein 1 in beige adipocytes in mice. *PLoS ONE*, *8*(12), 1–10. https://doi.org/10.1371/journal.pone.0084229

Porter, C. (2017). Quantification of UCP1 function in human brown adipose tissue. *Adipocyte*, *6*(2), 167–174. https://doi.org/10.1080/21623945.2017.1319535

Purdom, T., Kravitz, L., Dokladny, K., & Mermier, C. (2018). Understanding the factors that effect maximal fat oxidation. *Journal of the International Society of Sports Nutrition*, *15*(1), 1–10. https://doi.org/10.1186/s12970-018-0207-1

Ramsden, D. B., Ho, P. W. L., Ho, J. W. M., Liu, H. F., So, D. H. F., Tse, H. M., Chan, K. H., & Ho, S. L. (2012). Human neuronal uncoupling proteins 4 and 5 (UCP4 and UCP5): Structural properties, regulation, and physiological role in protection against oxidative stress and mitochondrial dysfunction. *Brain and Behavior*, *2*(4), 468–478. https://doi.org/10.1002/brb3.55

Reisi, J., Ghaedi, K., Rajabi, H., & Mohammad Marandi, S. (2016). Can resistance exercise alter irisin levels and expression profiles of fndc5 and ucp1 in rats? *Asian Journal of Sports Medicine*, *7*(4). https://doi.org/10.5812/asjsm.35205

Rodrigues, K. C. d. C., Pereira, R. M., de Campos, T. D. P., de Moura, R. F., da Silva, A. S. R., Cintra, D. E., Ropelle, E. R., Pauli, J. R., de Araújo, M. B., & de Moura, L. P. (2018). The role of physical exercise to improve the browning of white adipose tissue via POMC neurons. *Frontiers in Cellular Neuroscience*, *12*(March), 1–7. https://doi.org/10.3389/fncel.2018.00088

Roesler, A., & Kazak, L. (2020). UCP1-independent thermogenesis. *Biochemical Journal*, *477*(3), 709–725. https://doi.org/10.1042/BCJ20190463

Said, M. A., Abdelmoneim, M. A., Alibrahim, M. S., & Kotb, A. A. H. (2021). Aerobic training, resistance training, or their combination as a means to fight against excess weight and metabolic syndrome in obese students — which is the most effective modality? A randomized controlled trial. *Applied Physiology, Nutrition and Metabolism*, *46*(8), 952–963. https://doi.org/10.1139/apnm-2020-0972

Said, M. A., Alhumaid, M. M., Atta, I. I., Al-Sababha, K. M., Abdelrahman, M. A., & Alibrahim, M. S. (2022). Lower fitness levels, higher fat-to-lean mass ratios, and lower cardiorespiratory endurance are more likely to affect the body mass index of Saudi children and adolescents. *Frontiers in Public Health*, *10*. https://doi.org/10.3389/fpubh.2022.984469

Sanchez-Delgado, G., Martinez-Tellez, B., Olza, J., Aguilera, C. M., Gil, Á., & Ruiz, J. R. (2015). Role of exercise in the activation of brown adipose tissue. *Annals of Nutrition and Metabolism*, *67*(1), 21–32. https://doi.org/10.1159/000437173

Shirvani, H., & Arabzadeh, E. (2020). Metabolic cross-talk between skeletal muscle and adipose tissue in high-intensity interval training vs. moderate-intensity continuous training by regulation of PGC-1α. *Eating and Weight Disorders*, *25*(1), 17–24. https://doi.org/10.1007/s40519-018-0491-4

Simcox, J., Geoghegan, G., Maschek, J. A., Bensard, C. L., Pasquali, M., Miao, R., Lee, S., Jiang, L., Huck, I., Kershaw, E. E., Donato, A. J., Apte, U., Longo, N., Rutter, J., Schreiber, R., Zechner, R., Cox, J., & Villanueva, C. J. (2017). Global Analysis of Plasma Lipids Identifies Liver-Derived Acylcarnitines as a Fuel Source for Brown Fat Thermogenesis. *Cell Metabolism*, *26*(3), 509-522.e6. https://doi.org/10.1016/j.cmet.2017.08.006

Su, D., Jiang, T., Song, Y., Li, D., Zhan, S., Zhong, T., Guo, J., Li, L., Zhang, H., & Wang, L. (2025). Identification of a distal enhancer of Ucp1 essential for thermogenesis and mitochondrial function in brown fat. *Communications Biology*, *8*(1), 31. https://doi.org/10.1038/s42003-025-07468-3

Sugiharto, Sakti Adji, B., Merawati, D., & Pranoto, A. (2021). The increase of uncoupling protein-1 expression after moderate intensity continuous exercises in obese females. *Jurnal SPORTIF : Jurnal Penelitian Pembelajaran*, *7*(2), 194–205. https://doi.org/10.29407/js_unpgri.v7i2.15932

Sugiharto, Susanto, H., Andiana, O., & Merawati, D. (2019). Caloric Regulation Linked Thermogenesis in Acute Submaximal Intensity Exercise Model as the Effect of Audio Frequency Exposure. *IOP Conference Series: Materials Science and Engineering*, *515*(1). https://doi.org/10.1088/1757-899X/515/1/012069

Takaishi, K., Oshima, T., Eto, H., Nishihira, M., Nguyen, S. T., Ochi, R., Fujita, N., & Urakawa, S. (2021). Impact of exercise and detraining during childhood on brown adipose tissue whitening in obesity. *Metabolites*, *11*(10). https://doi.org/10.3390/metabo11100677

Vidal, P., & Stanford, K. I. (2020). Exercise-Induced Adaptations to Adipose Tissue Thermogenesis. *Frontiers in Endocrinology*, *11*(April), 1–12. https://doi.org/10.3389/fendo.2020.00270

Wang, W., & Seale, P. (2016). Control of brown and beige fat development. *Nature Reviews Molecular Cell Biology*, *17*(11), 691–702. https://doi.org/10.1038/nrm.2016.96

Wibawa, J. C., Arifin, M. Z., & Herawati, L. (2021). Ascorbic Acid Drink after Submaximal Physical Activity can Maintain the Superoxide Dismutase Levels in East Java Student Regiment. *Indian Journal of Forensic Medicine & Toxicology*, *15*(3), 3383–3392. https://doi.org/10.37506/ijfmt.v15i3.15824

Xiao, M., Zhang, Y., & Xu, X. (2023). Calorie Restriction Combined with High-Intensity Interval Training Promotes Browning of White Adipose Tissue by Activating the PPARγ/PGC-1α/UCP1 Pathway. *Alternative Therapies in Health and Medicine*, *29*(3), 134–139.

Yin, R., Ma, Y., Zhang, N., Yang, L., & Zhao, D. (2022). Combined effects of voluntary running and liraglutide on glucose homeostasis, fatty acid composition of brown adipose tissue phospholipids, and white adipose tissue browning in db/db mice. *Chinese Journal of Physiology*, *65*(3), 117–124. https://doi.org/10.4103/cjp.cjp-87-21

Zhu, Y., Qi, Z., & Ding, S. (2022). Exercise-Induced Adipose Tissue Thermogenesis and Browning: How to Explain the Conflicting Findings? *International Journal of Molecular Sciences*, *23*(21). https://doi.org/10.3390/ijms232113142

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