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PHYSIOLOGICAL REGULATION OF PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR-GAMMA COACTIVATOR 1 ALPHA IN MITOCHONDRIAL METABOLISM DURING PHYSICAL EXERCISES: A SYSTEMATIC REVIEW

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Abstract. Physiological regulation of peroxisome proliferator-activated receptor-gamma coactivator 1 alpha in mitochondrial metabolism during physical exercises: a systematic review. Ayubi N., Wibawa J.C., Rizki A.Z., Afandi A., Callixte C. *This study aims to analyze in depth the mechanism of physical exercises in increasing the expression of PGC-1α (peroxisome proliferator-activated receptor gamma coactivator 1-alpha) as the most important* *part of mitochondrial biogenesis through a systematic review. Literature databases including PubMed, Web of Science, and Science Direct were searched for this systematic review study. The inclusion criteria for this study were articles published in the last five years. The articles discussed PGC-1α, exercises, and mitochondrial biogenesis. PubMed, Web of Science, and Science Direct databases were used to find 141 published articles. Finally, 13 articles that met the inclusion criteria were selected and analyzed for this systematic review. In this study, standard operating procedures were evaluated using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Exercises have been shown to increase PGC-1α expression, according to this systematic review. Increased biogenesis in mitochondria may be triggered by increased PGC-1α expression, which helps in the energy production process. On the other hand, it is not yet clear about the ideal intensity and type of physical activity to increase PGC-1α. This provides recommendations for further exploration in future experimental studies.*

Реферат. Фізіологічна регуляція 1 альфа-коактиватора гамма-рецепторів, що активуються пероксисомним проліфератором, в мітохондріальному метаболізмі під час фізичних вправ: систематичний огляд. Аюбі Н., Вібава Дж.К., Різкі А.З., Афанді А., Каллікст К. *Це дослідження спрямоване на глибокий аналіз механізму фізичних вправ для підвищення експресії PGC-1α (peroxisome proliferator-activated receptor gamma coactivator 1-alpha) як найважливішої частини мітохондріального біогенезу шляхом систематичного огляду. Для цього систематичного оглядового дослідження було проведено пошук у базах даних літератури, включаючи PubMed, Web of Science і Science Direct. Критеріями включення до цього дослідження були статті, опубліковані за останні п'ять років. У статтях обговорювалися PGC-1α, фізичні вправи та мітохондріальний біогенез. За результатом пошуку в базах PubMed, Web of Science та Science Direct було знайдено 141 статтю. Для цього систематичного огляду було відібрано та проаналізовано 13 статей, які відповідали критеріям включення. У цьому дослідженні стандартні операційні процедури були оцінені з використанням переважних елементів звітності для систематичних оглядів і метааналізів (PRISMA). У цьому систематичному огляді було показано, що фізичні вправи збільшують експресію PGC-1α. Посилення біогенезу в мітохондріях може бути викликано підвищеною експресією PGC-1α, яка допомагає в процесі виробництва енергії. З іншого боку, ще не визначено оптимальну інтенсивність та тип фізичної активності для збільшення PGC-1α, що є важливим та може бути рекомендованим для подальших досліджень у майбутніх експериментальних дослідженнях.*

A hazardous metabolic syndrome, diabetes mellitus is typified by persistently high blood glucose levels brought on by the inability of the hormone insulin to be generated [1]. Diabetes mellitus occurs regardless of age, gender, and geographical location, all can be affected by this illness, which is the most common the world's leading cause of death. More than 90% of instances of environmental and genetic factors combine to develop type 2 diabetes mellitus [1].

The International Diabetes Federation (IDF) reports that the proportion of individuals with diabetes mellitus globally has reached a pandemic with sufferers in 2019 amounting to 9% of the total world population or around 463 million individuals [2]. The occurrence of diabetes mellitus can also lead to an increase in individuals suffering from heart disease and ischemic stroke, which are the main and second leading causes of disease burden worldwide in 2019 [3]. Insulin resistance and hyperglycemia are hallmarks of type 2 diabetes mellitus, a metabolic disorder [4].

Type 2 diabetes mellitus prevalence has increased, triggered by many factors that have become a habit of life in this modern era, including people rarely doing physical activity, often overeating consuming fast food so that it is experiencing an epidemic phase throughout the world [5]. Without preventive measures, the global prevalence of type 2 diabetes mellitus will increase to 592 million by 2035 [6].

The transcription factor known as peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) is recognized to be crucial for mitochondrial biogenesis, regulation of mitochondrial function, and control of ROS (reactive oxygen species) (McMeekin et al., 2021). PGC-1α plays a key role in the body's metabolism through regulation of mitochondria as a storehouse of energy production and contributes significantly to the gluconeogenesis process [8]. Mitochondria are very important organelles because they have the main function as an energy generation source for all eukaryotic cells and the amount of energy produced by mitochondria is abundant in organs such as the heart that need energy to function. Any activity that affects the work of mitochondria including mechanisms of biogenesis, cell repair, and mitophagy, all of these have a close function on the continuity of the work of mitochondria [9].

Additionally, PGC-1α is crucial for protein synthesis and fatty acid absorption, which are first initiated and controlled by the protein kinase adenosine monophosphate-activated (AMPK) [10]. It can be concluded that PGC-1α plays a crucial role in metabolism, especially in mitochondria as cell organelles that function for energy storage and energy production. In patients with diabetes mellitus, PGC-1α expression decreases, especially in patients with risk factors for heart disease [11]. So, this will worsen the condition of human health, especially of people with diabetes mellitus and can result in death if there is no effort in prevention.

Exercises is the best non-pharmacological therapy in improving human health by lowering the chance of heart disease, increasing insulin sensitivity, reducing obesity, improving lipid profiles and preventing diabetes mellitus [12]. Especially in patients with diabetes mellitus, exercises are highly recommended but must also be in accordance with established procedures and guidelines. In addition, it must also be in accordance with the doctor's recommendations in the intervention. During exercises, there are extraordinary and very complex physiological mechanisms in the human body ranging from increased skeletal muscle contraction and increased muscle mass [13], heart health improvement [14], repair and regeneration of cells and tissues [15], as well as other improvements that especially have a positive influence on the human body. Previous studies have reported that exercises are beneficial in increasing the expression of PGC-1α which plays a crucial role in the human body [16]. However, until now the underlying mechanism of the increase in PGC-1α during exercises has not been explained in detail. The optimal duration, type, and intensity of exercises in increasing PGC-1α still need to be analyzed.

This study aims to analyze in depth the mechanism of physical exercises in increasing the expression of PGC-1α as the most important part of mitochondrial biogenesis through a systematic review.

MATERIALS AND METHODS OF RESEARCH

This type of research is a systematic review. It searches journal databases, including PubMed, Web of Science, and Science Direct. Because these platforms collect papers with a strong scientific basis and influence, they are considered the best in the world.

The inclusion criteria for this study were established by examining articles published in the last five years that discussed PGC-1α and exercises. In addition, articles that did not meet the criteria for scientific validity or were not listed in search indexes such as PubMed, Web of Science, and Science Direct were excluded from our analysis.

Full text, abstract, and verified article titles were added to the Mendeley database. This study was conducted from October to December 2024 by searching the selected databases. In the first stage, 141 articles were found using PubMed, Web of Science, and Science Direct databases. For the second screening stage, 107 articles were selected that met the abstract and title requirements. Furthermore, 31 articles received requests for additional processing in the third stage. At this stage, we sorted them based on overall suitability. After careful examination and observation, thirteen publications were selected for analysis after meeting the inclusion criteria. The operational criteria for this investigation were to comply with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) evaluation (Fig. 1).

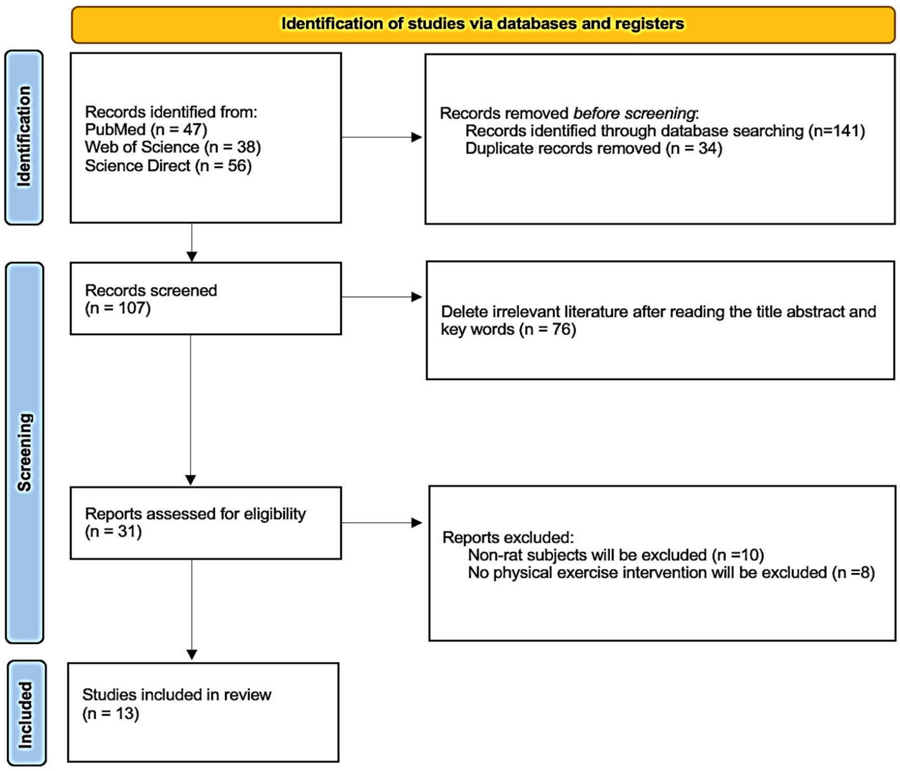

Fig. 1. PRISMA flowchart of the article selection process

RESULTS AND DISCUSSION

Summary of the design and intervention of the studies

Author	Design	Participants	Participants Age	Intervention	Outcome
(de Sousa Fernandes et al., 2022) [17]	Randomized Controlled Trial	12 male mice	8 weeks old	Aerobic exercises training Training was performed 5x per week, at 60% of maximal capacity, without incline, for 60 minutes per session. Training was conducted for eight weeks.	The group receiving physical activity intervention showed a significant increase in PGC-1α expression. Measuring tools: analysis of quantitative real-time polymerase chain reaction (qRT-PCR).
(Hejazi et al., 2020) [18]	Randomized Controlled Trial	24 male rats	weeks old	Moderate intensity Aerobic exercises For eight weeks, the mice participated in five weekly bouts of high- and moderate-intensity cardiovascular exercises lasting 60 minutes each. Rats in the moderate effort group can run 28 meters per minute (70% to 75% VO_2max) on a treadmill. High intensity aerobic exercises Rats at 34 meters per minute (80% to 85% VO_2max) in the high-intensity group.	Compared to the control group without intervention, PGC-1α expression was significantly higher in the groups that engaged in high-intensity and moderate-intensity aerobic activity. Measuring tools: special rat ELISA Kit.
(Gahramani & Karbalaeifar, 2019) [19]	Randomized Controlled Trial	12 male wistar rats	weeks old	High intensity interval training The training regimen included interval running on a treadmill for 30 minutes. Each alternation comprised two minutes of active recovery at 50–60% VO_2 max and four minutes of running at 90–90% VO_2 max. For eight weeks, training took place three days a week.	PGC-1α expression was significantly higher in the slow twitch and fast twitch groups than in the intervention-free control group. Measuring tools: analysis of quantitative real-time polymerase chain reaction (qRT-PCR).
(Shirvani et al., 2019) [20]	Randomized Controlled Trial	32 male rats	8 weeks old	Eccentric resistance training The eccentric resistance training exercises is performed using stairs. The ladder's design forces the rat to descend while maintaining a steady weight. To vary the intensity, the rats made 10-12 dynamic movements (repetitions) during each landing. The rats used a weighted backpack to complete the stair descending activity. The following is how the exercises is weighted: A repetition of the stair exercises was performed at 50%, 75%, 90%, 100%, and 120% of one repetition maximum (1 RM, which is equivalent to 50% of the rat's body mass), after 30 g was raised for each trial up to a maximum of eight trials. For six weeks, three sessions of 25 minutes each of eccentric resistance training were conducted.	PGC-1α expression significantly increased in the group with eccentric resistance training intervention than the control group without intervention. Measuring Tools: Analysis of quantitative real-time polymerase chain reaction (qRT-PCR).

Author	Design	Participants	Participants Age	Intervention	Outcome
(Hoseini et al., 2024) [21]	Randomized Controlled Trial	56 male wistar	10-12 weeks old	Aerobic training Mice run on a treadmill. It was determined that a running speed range of 20-25 m/min was suitable for aerobic training, producing an intensity level that would result in rats consuming 70-75% of their maximum oxygen intake. For eight weeks, this study employed a training regimen that included aerobic exercises on a treadmill five days a week.	PGC-1α expression significantly increased in the group with aerobic training + vitamin D intervention both high dose and moderate dose than the group with no aerobic training. Measuring tools: immunoblotting
(Guo et al., 2024) [22]	Randomized Controlled Trial	70 male rats	4 weeks old	Swimming exercises Rats were trained to swim in the pool for eight weeks, which had 40-45 cm of water at 30-32˚C. Rats in the diabetes + exercise group was given an extra load to swim with for a week prior to swimming training. For eight weeks in a row, rats in the diabetes + exercise group trained to swim for 60 minutes every day, five days a week.	The diabetes + exercise intervention group's PGC-1α expression was significantly higher than that of the diabetes alone group. Measuring tools: analysis of quantitative real-time polymerase chain reaction (qRT-PCR).
(Ebrahimnezhad et al., 2023) [6]	Randomized Controlled Trial	28 male wistar rats	8 weeks old	High intensity Interval training The mice spent five days getting to know the treadmill. Rats initially adjusted by running for ten minutes a day at a pace of eight meters per minute on a treadmill. Eight weeks of HIIT training.	The group receiving physical activity intervention showed a significant increase in PGC-1α expression. Measuring tools: western blot
(Ghadery et al., 2020) [23]	Randomized Controlled Trial	21 male wistar	8 weeks old	High intensity Interval training Three weekly sessions of HIIT training. The training lasts for six weeks. The exercises consisted of 5 sets of alternation, 1 minute of training, 1 minute of rest on the treadmill at 80% to 95% Vo2max intensity, and slow alternation at 55% Vo2max intensity in order to reach 10 sets of alternation in the final week. The rats warmed up and cooled down before and after training by running for five minutes at 40% Vo2max exercises.	The group receiving physical activity intervention showed a significant increase in PGC-1α expression. Measuring tools: analysis of quantitative real-time polymerase chain reaction (qRT-PCR).
(Shoghi et al., 2024) [24]	Randomized Controlled	42 male wistar rats	-	Moderate intensity training Mice running on a treadmill. The training regimen consists of a 10-meter run, a 5-minute warm-up, and a 10-minute cool-down. During the first week, the rats ran for 31 minutes at 55% of their full capacity. The following was the training protocol: 31 minutes at 19 m/min in week one, 31 minutes at 21 m/min in week two, 37 minutes at 23 m/min in week three, 40 minutes	The group receiving physical activity intervention showed a significant increase in PGC-1α expression. Measuring tools: analysis of quantitative real-time polymerase chain reaction (qRT-PCR).

Author	Design	Participants	Participants Age	Intervention	Outcome
				at 24 m/min in week four, 46 minutes at 24 m/min in week five, and 46 minutes at 26 m/min in week six.	
(Sylviana et al., 2019) [25]	Randomized Controlled	20 male wistar rats	10-11 weeks old	Moderate intensity training Mice running on a treadmill. The mice run at a speed of 20m/sec for 30 minutes. Exercise intensity 50%-70% VO_2Max. Exercises were carried out according to each intervention group, there were 3 days, 6 days, and 15 days of intervention. Exercise intervention is done 5 times a week.	The group that received a 15-day physical activity intervention showed a significant increase in PGC-1α expression. Measuring tools: analysis of quantitative real-time polymerase chain reaction (qRT-PCR).
(Cho et al., 2021) [26]	Randomized Controlled	20 male mice	14-16 weeks old	Acute swimming exercises Rats were acclimatized for 5 minutes per day for a week. Rats performed acute swimming for 90 minutes in an environment with a depth of more than 15 cm.	The group receiving physical activity intervention showed a significant increase in PGC-1α expression. Measuring tools: analysis of quantitative real-time polymerase chain reaction (qRT-PCR).
(Chou et al., 2024) [27]	Randomized Controlled	50 male mice	6 weeks old	Aerobic exercises Run 15 meters per minute on a treadmill. Exercises are performed for 40 minutes. Resistance exercises Run by climbing a ladder while bearing weight. The load is increased every week. Rats climbed 4x per set for a total of 3x repetitions of each exercise. Rest intervals were 2 minutes. High Intensity Interval Training Spend ten minutes running at a pace of five to seven meters per minute on a warm-up treadmill. After that, increase by running for 10 rounds a day for 1 minute at a speed of 18-20 m/min and 2 minutes at a speed of 10-12 m/min.	The group receiving aerobic exercises intervention showed a significant increase in PGC-1α expression. Measuring tools: analysis of quantitative real-time polymerase chain reaction (qRT-PCR).
(Luo et al., 2020) [28]	Randomized Controlled	45 male mice	8 weeks old	Aerobic exercises Mice sprint 8 meters per minute on a treadmill. The intervention was carried out for 30 minutes each exercise. On the fourth day, the incline was constant but the pace was raised to 10 meters per minute. After that, the rats ran on the treadmill once a day, 60 minutes at a time, six times a week for six weeks.	The group receiving aerobic exercises intervention showed a significant increase in PGC-1α expression. Measuring tools: analysis of quantitative real-time polymerase chain reaction (qRT-PCR).

Description of physical exercises increasing PGC-1α expression included in review

Conducted systematic review shows that expression of peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) rises with physical activity. The degree of expression is influenced by the kind, length, and intensity of exercises (PGC-1α). The interventions carried out were on average of moderate to high intensity, in addition there were also types of interval training and resistance training which all had a favorable impact on raising PGC-1α expression.

Considering the thirteen items that have been examined, all of them showed an increase in PGC-1α after physical exercise intervention (de Sousa Fernandes et al., 2022, Hejazi et al., 2020, Gahramani & Karbalaeifar, 2019, Shirvani et al., 2019, Hoseini et al., 2024, Guo et al., 2024, Ebrahimnezhad et al., 2023, Ghadery et al., 2020, Shoghi et al., 2024, Sylviana et al., 2019, Cho et al., 2021, Chou et al., 2024, Luo et al., 2020). In addition, the data also show that the provision of physical exercise intervention begins with exercises adaptation first, then core exercises. The exercise interventions used are also diverse, consisting of high-intensity interval training, endurance training, aerobic exercises, resistance training, all of which showed a positive increase in PGC-1α expression post-intervention.

This study focused on the observation of increased PGC-1α expression due to physical exercises. Articles that did not discuss this were included in the exclusion criteria, and were not included in this systematic analysis. Papers that discussed how moderate or vigorous intensity physical exercises or resistance exercises types increased PGC-1α expression were included in the inclusion criteria for further discussion. So according to the examined articles it can be concluded that PGC-1α expression significantly increased following physical activity.

Effect of exercises intensity on increasing PGC-1α expression

Exercise intensity has different effects regarding the rise on PGC-1α. We all know that engaging in physical activity benefits health status improving. The data show and compare aerobic exercises of moderate intensity and high intensity, aerobic exercises which both provide a significant increase in PGC-1α expression, the exercises are done with a duration of 60 minutes per session, five weekly sessions were conducted for eight weeks of intervention [18]. Rats given aerobic activity five times a week for eight weeks, lasting 60 minutes each, likewise demonstrated a substantial increase in PGC-1α expression [17].

Other data proving that there is an elevation in PGC-1α expression in rats that were intervened by high intensity interval training were also conveyed by Gahramani & Karbalaeifar, 2019. Another type of exercises and interventions, namely eccentric resistance training performed on rats with a duration of 25 minutes per session, 3x a week for 6 weeks of treatment also proved that there was an increase in PGC-1α [20]. Exploration related to the comparison of exercise types on influencing PGC-1α expression needs to be explored further, data that have been found comparing several types of physical exercises including aerobic exercises, resistance exercises, and high intensity interval training show that aerobic exercises significantly increase physical perfomance [27]. However, to strengthen which type of physical exercises is effective in increasing PGC-1α expression needs to be further explored in subsequent experimental studies.

In addition to physical exercises, it turns out that vitamin D supplementation combined with exercises can also have a significant effect on increasing PGC-1α expression, but the mechanism underlying vitamin D and exercises in increasing PGC-1α needs to be explained [21]. It is also still a matter of confusion because of the complexity of what happens within the cell when the body performs physical exercises. The underlying signal transduction pathways need to be deepened and researched. In patients with diabetes mellitus exercises are the best non-pharmacological therapy to reduce hyperglycemia. Research data of Guo et al., 2024. This study, which compared rats with induced diabetes given physical exercise intervention and not given physical exercises, revealed a notable rise in PGC-1α in the diabetes mellitus group given physical exercise intervention.

Training with the type of high intensity interval training also has a positive effect on increasing PGC-1α. Data by Ebrahimnezhad et al., 2023 have shown that rats that have been given a high intensity interval training intervention conducted for 8 weeks are proven to increase the expression of PGC-1α after the intervention. This data are also reinforced by Ghadery et al., 2020 who observed that during an 8-week period of high intensity interval training three times a week, PGC-1α expression increased favorably. Every analysis has demonstrated that physical activity positively affects PGC-1α expression, a key precursor in mitochondrial biogenesis.

The purpose of this systematic review was to determine the effects of physical activity in increasing PGC-1α expression. Peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α) is described as a key regulator in the process of biogenesis in mitochondria, so it is important to discuss

[29]. By giving proteins with histone acetyltransferase activity a docking platform, PGC-1α functions more as a transcriptional regulator. Consequently, PGC-1α indirectly facilitates the transcription [30].

During physical exercises, physiologically the human body's skeletal muscles in particular increases reactive oxygen species (ROS) [31]. Exercise is another frequent stressor that causes a shortage in oxygen supply, which makes it impossible for the body to meet the rapidly increasing oxygen demand. This causes many tissues and organs to produce a number of highly active molecules, including reactive oxygen species (ROS) and reactive nitrogen species (RNS) [32]. The emergence of ROS will affect other signal transduction. The increase in ROS during exercises is certainly something that has long been discussed and this is very natural since it is a physiological reaction to physical activity. The increase in ROS also increases the levels of antioxidants such as superoxide dismutase (SOD) in the body [33].

The signal transduction pathway that activates PGC-1α expression starts from ROS which affects the increase of adenosine monophosphate-activated protein kinase (AMPK) [34]. Adenosine monophosphate-activated protein kinase (AMPK) in muscle cells specifically functions to bind PGC-1α [35]. Moreover, this phosphorylation is required for AMPK-induced mitochondrial gene expression [36]. Remarkably, PGC-1α plays a part in mitophagy and mitochondrial dynamics in addition to controlling mitochondrial biogenesis [37]. This interaction can occur in a variety of ways. PGC-1α can first directly bind and activate AMPK to increase its kinase activity [38]. Second, PGC-1α promotes the expression of AMPK signaling-targeted genes involved in fatty acid oxidation [39].

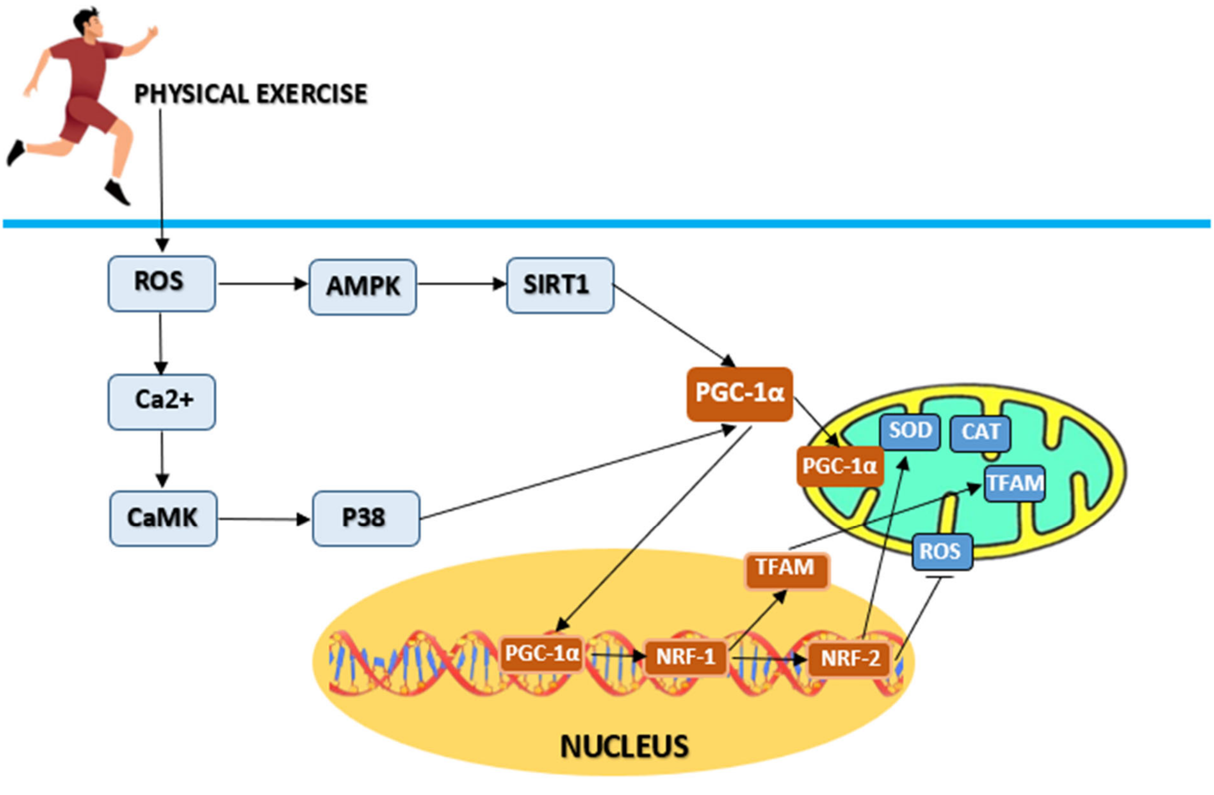

Fig. 2. The mechanisms of physical exercises in increasing PGC-1α expression

Sirtuin 1 is known to deacetylate various prominent transcription factors and proteins activated by AMPK [40]. This activated SIRT1 influences the response of increased expression of PGC-1α [41]. Sirtuin 1 (SIRT1) and AMPK, crucial regulators in the regulatory network for metabolic homeostasis, lie at the heart of the elevated production of PGC-1α [42]. Given the complexity of the SIRT1 response to exercises, it's critical to determine how exercise intensity, kind, or duration may impact SIRT1 levels both acutely (during a single bout) and after multiple exercise sessions [43]. In addition to SIRT1 in the control of PGC-1α there is also SIRT3, a mitochondrial deacetylase that affects PGC-1α [44]. SIRT3 may affect glucose metabolism that occurs in the mitochondria [45]. However, the explanation of SIRT3 in its effect on PGC-1α increase needs to be further explored along with the stages that influence it.

In another pathway, exercise-induced ROS is also a physiological response that can make calcium ions

(Ca^{2+}) increase [46]. Increased Ca^{2+} will trigger increased expression of calmodulin-dependent protein kinase (CaMK) which is a physiological response arising from physical exercises [47]. Increased muscle contraction during physical exercises leads to increased expression of p38 mitogen-activated protein kinase [48]. This increase in p38 will trigger the expression of PGC-1α [49]. In fact, the inflammatory response is exacerbated if PGC-1α activation is reduced in an inflammatory body condition because of elevated cytokine levels [29]. The transport of SIRT1 and PGC-1α into the mitochondria, where they form a complex with the mtDNA region responsible for controlling mitochondrial DNA replication and transcription, is believed to be facilitated by activated PGC-1α acting as a coactivator for mitochondrial transcription factor (TFAM) [29]. So, the increased expression of PGC-1α will have a key influence in the process of biogenesis in mitochondria [50].

So, it is known that physical activity has a beneficial impact on improving biogenesis mechanisms in mitochondria. Research data by Sylviana et al., 2019 have shown that physical exercises performed on rats with moderate intensity for 15 days of treatment provides evidence of a notable rise in the expression of PGC-1α. In addition, other studies in rats that have been given swimming intervention for 90 minutes show that there is a notable rise in PGC-1α following the intervention [26]. Subsequent data also showed that there was an increase in PGC-1α in rats that had been given a physical exercise intervention for 60 minutes per session, 6x a week for 6 weeks of intervention [41]. Overall, it is evident that exercises is the best non-pharmacological therapy in an effort to improve the body to stay healthy through the mechanism of increasing PGC-1α expression as a precursor of biogenesis in mitochondria.

Strenght and Limitations

This systematic review has the benefit of focusing only on randomized controlled trials, which are the most trustworthy source of scientific data because there is no chance of ambiguous causal linkages. To ensure that all samples displayed consistent data and were not contaminated with data from other animal or human categories, the samples were also exclusively focused on animals. Regular exercises and their effect on elevating PGC-1α expression after exercises are very relevant to the thorough examination of its function in order to suggest exercises as the most effective means of enhancing the mitochondrial biogenesis process.

The drawback we found is that, even though regular physical exercises can improve human life quality by enhancing the biogenesis mechanism in mitochondria through increased PGC-1α expression, there are extremely few recent studies that address this issue and demonstrate the positive effects of this increase in PGC-1α expression following physical exercises. An additional constraint is that this review only covers the method by which physical activity increases PGC-1α expression. Of course, more research is still needed to fully understand the molecular and signal transduction phases of the specifics or other expression factors that take place within the cell. This is necessary to respond to the phases in the extremely mechanism of physical activity.

CONCLUSION

Based on the analysis of this systematic review, it can be concluded that physical activity can increase the expression of PGC-1α after exercises. This increase will affect the body's metabolism because it causes biogenesis in the mitochondria.

Contributors:

Ayubi N. – conceptualization, validation, formal analysis, resources, writing – original draft, writing – review & editing, visualization, project administration, funding;

Wibawa J.C. – methodology, software, validation, investigation, resources, data curation, supervision, writing – original draft, writing – review & editing;

Rizki A.Z., Afandi A., Callixte C. – validation, resources, writing review & editing;

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