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Does Resistance Training Have Positive Effects on Redox Homeostasis in the Human Body?

Literature Review

Regular aerobic or resistance training is associated with better body composition, physical and mental health, and reduced all-cause mortality. Physical exercise also lowers the risk for diseases that relate to chronic oxidative stress like cancer, diabetes, and neurodegenerative disorders. Paradoxically, exercise induces oxidative stress in the body. This review investigates whether highly demanding resistance training positively impacts redox homeostasis in the human body. From the studies reviewed here, it can be concluded that regular resistance training results in training adaptations of the antioxidant system, enabling the body to cope better with future oxidative stress induced by exercise or other bodily or environmental factors. This effect has been demonstrated over different ages, genders, health statuses, as well as resistance training intensities. Thus, it should be recommended as a general health behavior for the prevention and potential therapy of a wide range of diseases. This review is limited by the small number of reviewed studies. Further, a

comparison between studies is difficult due to the variety of subjects. Nonetheless, a positive effect of resistance training on redox homeostasis could be consistently reported.

Keywords: oxidative stress, resistance training, physical exercise, redox homeostasis

INTRODUCTION

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It is common knowledge that an active lifestyle with regular physical exercise benefits the health of the body and mind. Physical activity has been related to improved mood and body composition – measured in muscle mass, fat mass, or BMI. In addition, physical activity is associated with a reduction in all-cause mortality, particularly by reducing the risk of common (fatal) diseases like cardiovascular disease, diabetes, cancer, and Alzheimer's disease (Blair et al., 2001; Crespo et al., 2002; Hendrix et al., 2020; Kraemer et al., 2002; Oguma et al., 2002; Penedo & Dahn, 2005; Powers et al., 2020; Westcott, 2012; Winett & Carpinelli, 2001). Many of those common diseases, like cancer, diabetes, as well as neurodegenerative disorders like Parkinson's disease and Alzheimer's disease, are related to chronic oxidative damage (Finaud et al., 2006; Powers et al., 2020; Valko et al., 2007). Excessive oxidative stress causes oxidative damage.

Oxidative stress refers to a disruption of redox homeostasis, referring to the balance between pro-oxidants (oxidizing agents) and antioxidants (reduction agents), due to an increase in pro-oxidants, which has detrimental effects on cell functioning. Pro-oxidants are prone to oxidize other molecules to become more stable. Hence, increases in oxidants that are not sufficiently scavenged by antioxidants results in oxidative damage - the oxidation of proteins, DNA, and lipids, impairing

their function and therefore leading to cell damage or death. Cell damage, especially damage to DNA, can cause mutations and altered gene expression which ultimately induces and perpetuates diseases like cancer (Finaud et al., 2006; Hendrix et al., 2020; Powers et al., 2020; Powers & Jackson, 2008; Valko et al., 2007).

Regular physical exercise has been shown to reduce the risk of diseases related to oxidative stress (Crespo et al., 2002; Powers & Jackson, 2008; Winett & Carpinelli, 2001). Paradoxically, an acute bout of physical exercise increases the generation of reactive oxygen species (ROS), a subset of oxidants that contain oxygen and are highly reactive. ROS, like other pro-oxidants, can damage DNA, lipids, and proteins, by oxidizing them. An increase in ROS, if not sufficiently counteracted by an increase in antioxidants leads to oxidative stress and damage. Previous studies established that any form of physical exercise increases ROS since the contraction of muscles is associated with ROS production. Hence, exercise induces oxidative stress, which can lead to oxidative damage (Powers et al., 2020; Powers & Jackson, 2008). Still, despite, or maybe because of this exercise-induced oxidative stress, physical exercise has many positive effects on physical and mental health. Regular physical exercise induces several positive training adaptations relating to insulin resistance, metabolic rate, body composition, and cardiovascular fitness (Winett & Carpinelli, 2001). These training adaptations might extend to the redox system, leading to higher resilience and antioxidant capacity, and overall better regulation of redox homeostasis. Therefore, exercise could prepare the body to cope with otherwise induced oxidative stress, by "training" the antioxidant response. A trained antioxidant system could slow or prevent the detrimental effects of disorders associated with

oxidative stress, like Alzheimer's, cardiovascular disease, depression, and schizophrenia, as well as slow biological aging (Raza et al., 2016; Valko et al., 2007). In addition, it has been shown that a certain amount of ROS is necessary for cell signaling and immune function. Therefore, only a sustained highly oxidative environment will ultimately have negative effects on health (Finaud et al., 2006; Powers & Jackson, 2008).

To date, most research into exercise was performed on aerobic training, for example, running, swimming, or biking (Dilorenzo et al., 1999; Finaud et al., 2006; Roque et al., 2013; Tarumi & Zhang, 2014; Wilmore, 2003). However, there has been an increasing scientific interest in anaerobic or resistance training (RT). In RT, controlled voluntary muscle movements are performed against resistance, for example, body weight, free weights, or machines. Increasing evidence showed that the health effects of RT are comparable to those associated with aerobic training (Blair et al., 2001; Crespo et al., 2002; Kraemer et al., 2002; Westcott, 2012; Winett & Carpinelli, 2001). Both aerobic training and RT induce oxidative stress (Finaud et al., 2006). Still, both activities lead to considerable health benefits. RT is simple but versatile, efficient, and effective (Winett & Carpinelli, 2001). Therefore, it is highly suitable for health interventions in the general or patient population. Research must investigate which factors contribute to the positive effects of RT on the redox system. This allows a safe implementation of RT interventions for patients with diseases related to oxidative stress.

Firstly, in this review paper, it is explored whether RT leads to training-induced adaptations in the body's redox system and therefore facilitates redox homeostasis and antioxidant response. Secondly, it is investigated whether these benefits occur without additional detrimental

effects due to RT-induced oxidative stress. In addition, the effects of RT on different population groups – age, gender, and health status – are compared. Lastly, the influence of RT intensity is evaluated.

Oxidative stress

Oxidative stress can be defined as an increased ratio of pro-oxidants to antioxidants, which impairs redox signaling and control, and/or leads to molecular damage (Powers et al., 2020; Powers & Jackson, 2008). ROS are a subset of pro-oxidants that contain oxygen and have unpaired electrons or are highly unstable. They are highly reactive because they achieve a more stable state by oxidizing other molecules. ROS are prone to oxidize cell or mitochondrial DNA, lipids, and (misfolded) proteins which damages those molecules and impairs their functioning in the cell. This in turn can induce apoptosis, inflammation, or altered cellular function. (Finaud et al., 2006; Valko et al., 2007). The oxidation of lipids in the cell membrane compromises the integrity of the cell and increases membrane permeability. Protein oxidation can damage the structure of proteins and enzymes, thus altering their function and impairing processes like genetic transcription. ROS can also damage DNA and cause strand breaks which increases the chance of harmful mutations and contributes to cell aging and cancer (Finaud et al., 2006). Oxidative damage has been related to common diseases, including cancer, cardiovascular disease, diabetes, and neurodegenerative diseases, like Parkinson's and Alzheimer's (Finaud et al., 2006; Powers et al., 2020; Valko et al., 2007) as well as mental disorders, like depression, bipolar disorder, and schizophrenia (Raza et al., 2016).

The production of ROS is a byproduct of cell metabolism that occurs naturally in the body. The presence of ROS is not inherently negative and does not inevitably lead to oxidative damage. Research showed that low-to-moderate amounts of ROS are essential for immune function, cell signaling, enzyme activation, drug detoxification, glycogen repletion, apoptosis, and muscle force production (Finaud et al., 2006; Powers et al., 2020; Powers & Jackson, 2008). Therefore, a redox imbalance in favor of the antioxidant side also has detrimental effects on health. For example, it can favor the growth of cancer because cancer cells are inhibited from programmed cell death (apoptosis). ROS are continuously scavenged by bodily enzymatic and non-enzymatic as well as nutritional antioxidants to achieve homeostasis and prevent oxidative damage (Finaud et al., 2006; Powers & Jackson, 2008; Valko et al., 2007). The most commonly investigated antioxidants are superoxide dismutase (SOD), glutathione peroxidases (GPx), catalase (CAT), vitamin C, vitamin E, uric acid, and glutathione (GSH). Therefore, a large increase in ROS production does not necessarily lead to oxidative damage if the ROS are sufficiently counteracted by antioxidants. Thus, it is desirable to have a flexible antioxidant system that can upregulate antioxidant production to accommodate spontaneous increases in ROS while avoiding continuously high antioxidant levels that prevent the signaling and immune functions of ROS (Powers & Jackson, 2008).

Different markers are used to assess ROS, oxidative damage, and antioxidant capacity. The most widely used markers for oxidative damage are malondialdehyde (MDA) or PEROX for lipid peroxidation, carbonyl groups for protein oxidation, 8-OH-dG for DNA oxidation, and GSH/GSSH ratio for overall oxidative stress (Finaud et al., 2006; Powers

& Jackson, 2008; Valko et al., 2007). Measuring ROS directly and reliably is difficult because of their short half-lives. Therefore, most studies use the markers of oxidative damage listed above. For measuring antioxidant capacity, the most common markers are SOD and total antioxidant capacity. The levels of all the antioxidants mentioned above (CAT, GPx, uric acid…) can be directly measured since they are constantly present in cells. In conclusion, the deciding factor for health or disease is the continuous balance between oxidants and antioxidants (redox homeostasis) as well as the total antioxidant capacity in response to spontaneous strong increases in oxidants.

Effects of resistance training on redox homeostasis

Various studies showed that physical activity of any kind increases ROS production, due to increased muscle contractions, cardiovascular activity, and metabolic rate (Belviranli & Gökbel, 2006; Diaba-Nuhoho et al., 2018; Finaud et al., 2006; Hendrix et al., 2020; Hudson et al., 2008; Powers et al., 2020; Powers & Jackson, 2008; Thirupathi et al., 2021). Increased body temperature and lactic acid are also related to the exercise-induced increase in ROS (Finaud et al., 2006). This exercise-induced oxidative stress can also lead to oxidative damage to proteins, lipids, and DNA. During aerobic exercise, the increased amount of ROS stem mainly from cell mitochondria (Finaud et al., 2006; Powers et al., 2020; Powers & Jackson, 2008; Valko et al., 2007). However, during RT, ROS are additionally produced during ischemia-reperfusion (Finaud et al., 2006). Ischemia-reperfusion occurs when the muscles are highly active – which is especially the case with high-intensity, high-resistance

training. Therefore, the blood flow is mainly directed to the muscle fibers, which leaves other tissues ischemic. After tension is released, blood flows back into the ischemic tissues quickly, which increases ROS and can result in tissue injury. Still, it is unclear what causes ROS during ischemia-reperfusion(Finaud et al., 2006).

The production of ROS increases with the intensity and duration of muscle force production. It is important to investigate the effects of RT on the redox system because RT is often performed at high intensities – often higher than aerobic activity – to either gain substantial amounts of muscle mass (hypertrophy), or to increase muscle endurance or strength. Training intensities usually vary between 70-90% of the one-repetition maximum (1RM) – that is the maximum load with which one can perform one repetition of the exercise. This high-intensity training increases the overall strain on multiple body systems, especially the muscle fibers and cardiovascular system. Therefore, higher intensity training should also increase ROS production to a greater extent, which might result in negative consequences. Research showed that with prolonged exercise ROS contribute to muscle fatigue. Furthermore, if exercise is excessive and nutritional antioxidants are insufficient, exercise-induced oxidative stress can lead to overtraining syndrome (Finaud et al., 2006; Hendrix et al., 2020; Powers & Jackson, 2008). However, despite the potential negative consequences of exercise-induced oxidative stress, ROS are necessary for muscle force production and thus essential for exercise. In addition, the presence or increase of ROS does not necessarily cause oxidative damage if they are sufficiently counteracted by an increase of antioxidants.

Previous research showed that regular aerobic training, and RT, result in several training adaptations which concern body composition, strength, mobility, metabolism, and cardiovascular adaptations (i.e., VO2max increase) (Blair et al., 2001; Bloomer et al., 2008; Kraemer et al., 2002; Powers et al., 2020; Westcott, 2012; Winett & Carpinelli, 2001). These training adaptations possibly extend to the redox system. Since exercise generates ROS through muscle contraction and ischemia-reperfusion it subjects the body to the stimulus of oxidative stress that originates as a by-product of the intense activity of healthy bodily systems (i.e., muscles). Thus, the body can "practice" its antioxidant response in a controlled and repeated way. Therefore, should toxins or diseases induce excessive oxidative stress, the body is prepared to react due to its increased antioxidant capacity. However, the exact mechanisms responsible for the inverse relationship between physical exercise and disorders related to oxidative stress remain elusive. In this review, eleven studies are compared, to investigate whether the training adaptations caused by regular RT include adaptations of the redox system In nine of those studies, subjects that had not performed RT in the past year participated in an RT intervention (Alikhani & Sheikholeslami-Vatani, 2019; Azizbeigi et al., 2013, 2015; Bloomer et al., 2008; Bobeuf et al., 2011; Cakir-atabek et al., 2010; Cook et al., 2013; Vezzoli et al., 2019; Vincent et al., 2006). The interventions comprised RT two-to-three times a week on non-consecutive days for around one hour, including a warm-up. The interventions lasted between six weeks and six months. The two remaining studies compared existing groups of inactive individuals with those who perform regular RT (Cakir-atabek & Ozdemir, 2015; Diaba-Nuhoho et al., 2018).

Eight studies investigated the effect of RT on markers of lipid peroxidation (MDA (Alikhani & Sheikholeslami-Vatani, 2019; Azizbeigi et al., 2013, 2015; Bloomer et al., 2008; Bobeuf et al., 2011; Cakir-atabek et al., 2010; Diaba-Nuhoho et al., 2018) or PEROX (Vincent et al., 2006)) as an indicator of oxidative damage. In six of those eight studies, RT decreased the investigated marker of lipid peroxidation. One study (Bobeuf et al., 2011) reported no significant difference. A study that compared active with inactive individuals (Diaba-Nuhoho et al., 2018) found increased MDA levels for vigorous exercisers.

To evaluate the body's ability to cope with an increase in ROS, five studies (Alikhani & Sheikholeslami-Vatani, 2019; Azizbeigi et al., 2013; Bloomer et al., 2008; Bobeuf et al., 2011; Vezzoli et al., 2019) assessed total antioxidant capacity (TAC), Trolox equivalent antioxidant capacity (TEAC), or total antioxidant status (TAS). Only two studies (Alikhani & Sheikholeslami-Vatani, 2019; Vezzoli et al., 2019) found an increase in the examined marker, while the rest indicated no difference between exercise or non-exercise groups or between pre-and post-intervention. Five studies measured SOD as an indicator of antioxidant capacity (Azizbeigi et al., 2013, 2015; Bloomer et al., 2008; Cakir-atabek & Ozdemir, 2015; Diaba-Nuhoho et al., 2018). All found an increase in SOD for the exercise group.

Overall, most of the studies showed a trend toward an increase in antioxidants, as well as a decrease in markers of oxidative damage. Only one study found an increase in lipid peroxidation for vigorous exercisers (Diaba-Nuhoho et al., 2018). However, the study compared active with inactive individuals and therefore had high variability in training protocols and intensities. Nevertheless, they found several other positive

effects of physical activity on overall health. Bobeuf et al. (2011) did not find any significant positive effects in a study that compared four groups: placebo control, vitamin C/E supplementation, RT, and combined RT and vitamin supplementation. However, the average sample size per group was only 14 participants and, consequently, the analysis had low statistical power. In addition, there was no increase in markers of oxidative damage.

The results of the RT interventions point towards positive effects of RT on the redox system: RT fosters healthy redox homeostasis, increases antioxidant capacity, and thus prevents oxidative damage and its negative consequences for health. For possible large-scale interventions, it is important to note, that the effects were consistently observed over a large variety of intervention durations between six weeks and six months, however, the effectiveness of shorter interventions cannot be guaranteed. Further, all intervention programs scheduled time for recovery and limit training to two to three times a week, which facilitates training adaptations and prevents the detrimental effects of excessive oxidative stress (Winett & Carpinelli, 2001).

The effects mentioned above were only observed in the most widely used redox markers, namely SOD and MDA. All studies used additional markers (TNF-α, uric acid, CAT, GPx, GSH). For those markers, there was either no effect or the effect was in the same direction as the effects on the markers mentioned above. It can be concluded that RT leads to an improvement in redox balance, namely a decrease in oxidants and an increase in antioxidants. However, these training adaptations are either specific for certain antioxidants and oxidants or

the effects are general but only measurable on the most prominent markers.

Effects of resistance training on different population groups

Four of the eleven studies examined the effect of RT on older adults (>54 years). Alikhani and Sheikholeslami-Vatani (2019) compared the effect of a 12-week RT protocol at 75% 1RM on younger (18-25 years) and older (55-65 years) women. They found that the antioxidant defense system is strengthened equally for both younger and older women. Bloomer et al. (2008) investigated the effects of an eight-week RT program on older adults (>54 years) with Parkinson's disease. The training was well tolerated, increased antioxidants (SOD, GPx), and decreased oxidative damage (H_2O_2, MDA). These adaptations might counteract the increase of oxidative stress caused by Parkinson's disease. Two studies (Vezzoli et al., 2019; Vincent et al., 2006) examined the effects of RT on obese, overweight, and sarcopenic older adults (>60 years) and found that long-term exercise reduced exercise-induced oxidative stress. In addition, RT served as a protection against cardiovascular risk factors. The improvements in the antioxidant defense system were correlated with an increase in strength and a reduction in body fat (Cakir- Atabek 2015). This suggests that redox adaptations are part of the overall training adaptations to regular RT. Training effects like a change in body composition are more easily observable than changes in the cellular redox system. A correlation between the two allows easier and cheaper monitoring of all RT adaptations, which can be useful for large-scale RT interventions. The eleven studies were performed on a highly diverse

subject pool in different countries with different ethnicities, ages, genders, and health statuses, yet all came to the same conclusion. This confirms the potential for RT interventions to be used as a health intervention for healthy as well as diseased people of all ages and backgrounds.

Comparing the effects of resistance training intensities

Research into RT has shown that there is an intensity threshold below which no or only neglectable training adaptations take place, concerning muscle mass, strength, body composition, and cardiovascular fitness (Winett & Carpinelli, 2001). Studies into exercise-induced oxidative stress suggest a similar threshold for the increase in oxidative stress. At moderate levels, increased ROS enable cellular signaling and immune defense; at high levels, ROS can lead to oxidative damage (Finaud et al., 2006; Hendrix et al., 2020; Powers et al., 2020; Powers & Jackson, 2008; Thirupathi et al., 2021). The threshold for non-redox adaptations is around 40-50% of either VO2max or 1RM. The experimental studies reviewed here used exercise intensities of 50-90% of (estimated) 1RM, thus all studies were above the threshold where training adaptations should take place. Two studies directly compared the effects of RT at different intensities. Azizbeigi (2015) found that an increase in antioxidant enzymes and a decrease in inflammatory markers following RT are independent of exercise intensity (85-90% of 1RM vs. 65-70% of 1RM). Similar results were observed by Cakir-atabek (2010), who compared strength (85% of 1RM) with hypertrophy (70% of 1RM) training. Both protocols significantly decreased MDA levels and

increased GSH. Other studies found a general dose-response relationship between RT and positive health as well as strength outcomes (Blair et al., 2001; Crespo et al., 2002; Winett & Carpinelli, 2001). At very high intensities, the dose-response function is reported to be either asymptotic (Blair et al., 2001) or declining (Powers et al., 2020; Powers & Jackson, 2008; Thirupathi et al., 2021). The latter hormesis function suggests that increased exercise intensity also increases oxidative stress, and therefore, training adaptations up to a certain maximum of exercise-limiting fatigue. Training at intensities beyond the threshold for training adaptations does not lead to greater benefits but instead undermines recovery and causes greater muscle fatigue, overtraining syndrome, and oxidative damage (Powers & Jackson, 2008; Winett & Carpinelli, 2001). Nevertheless, the studies reviewed here did not find negative effects for higher intensities, suggesting that this maximum point is not reached during regular and supervised training conditions with sufficient recovery intervals. Furthermore, the adaptive effects were found across the whole intensity spectrum from 50% to 90% of 1RM, which again confirms the high variability of effective RT protocols. All those intensities were above the hypothesized threshold for training adaptations. Thus, it cannot be concluded whether there is an intensity threshold for redox adaptations following RT.

DISCUSSION

This review examined the potential benefits of RT of different intensities on redox homeostasis in humans of different ages, gender, and health

status. To investigate that research question, eleven studies were compared. Nine of those studies performed RT interventions on previously untrained subjects (Alikhani & Sheikholeslami-Vatani, 2019; Azizbeigi et al., 2013, 2015; Bloomer et al., 2008; Bobeuf et al., 2011; Cakir-atabek et al., 2010; Cook et al., 2013; Vezzoli et al., 2019; Vincent et al., 2006). The remaining two studies compared regular exercisers with non-exercisers (Cakir-atabek & Ozdemir, 2015; Diaba-Nuhoho et al., 2018). The study pool included a wide range of participant backgrounds, intervention durations, and RT intensities. Overall, the findings are positive: consistent RT increases the body's ability to cope with oxidative stress by inducing training adaptations of the redox system. In addition, no negative effects – namely increased oxidative damage – have been found, even though exercise has been proven to induce oxidative stress.

Studies and reviews comparing regular exercisers with inactive people consistently show that an active lifestyle, also involving RT, is related to an increase in the antioxidant defense system (Belviranli & Gökbel, 2006; Cakir-atabek & Ozdemir, 2015; Diaba-Nuhoho et al., 2018), and an overall decrease in risk factors for diabetes, heart disease, cancer, and all-cause mortality (Blair et al., 2001; Crespo et al., 2002; Hendrix et al., 2020; Kraemer et al., 2002; Oguma et al., 2002; Penedo & Dahn, 2005; Powers et al., 2020; Westcott, 2012). However, it has been established oxidative stress is increased during and immediately after exercise. Nevertheless, more recent research suggests that the overall positive health benefits of physical exercise might be linked to the increased ROS production, since ROS aid cell signaling, immune function, and enzyme activation (Belviranli & Gökbel, 2006; Powers et al., 2020; Valko et al., 2007). In addition, the primary exercise-induced oxidative stress might

be necessary for the training adaptations. Consequently, if there is an adequate balance between oxidants and antioxidants – redox homeostasis – oxidative damage can be prevented while still allowing for training adaptations. Almost all the studies investigated here show that RT promotes healthy redox homeostasis, the capacity of the body to react sufficiently to short-term increases in oxidative stress and prevents oxidative damage. This also enables the body to prevent diseases related to chronic oxidative stress, or cope better with such diseases (Blair et al., 2001; Bloomer et al., 2008; Hendrix et al., 2020; Westcott, 2012; Winett & Carpinelli, 2001). Still, RT intensity might be an important factor to consider since other research suggested harmful effects of very high-intensity RT (Powers et al., 2020; Winett & Carpinelli, 2001). However, the wide range of intensities covered in this review, also representing all commonly used intensities, did not suggest a threshold in this normal range. Furthermore, all interventions lasted for a sufficient amount of time for training adaptations to take place. Even though the length of the interventions varied considerably between six weeks and six months, they did not differ in their effects, which supports the efficiency of RT. The training schedules all allowed enough time for recovery, which possibly contributed to the fact that no increase in oxidative damage was found since the body had enough time to recover from exercise-induced oxidative stress. Also, training two-to-three times a week seems to be enough to induce training adaptations.

The reviewed studies all point towards the overall positive health effects of RT as well as training adaptations of the redox system. The findings are in line with the overall preventive and therapeutic health benefits of physical exercise found in other studies (Crespo et al., 2002;

Westcott, 2012; Winett & Carpinelli, 2001), however, the mechanisms that lead to the redox adaptations still need to be investigated. In addition, the positive effects mentioned above were observed consistently over age, gender, health status, and training intensity, demonstrating that RT is safe for all kinds of people. It is efficient and effective (Westcott, 2012; Winett & Carpinelli, 2001). Therefore, RT is suitable for large-scale preventive health interventions for the general population. In addition, RT could supplement drug therapy for many common diseases. RT has also been shown to have positive effects on neurodegenerative diseases and mental disorders (Penedo & Dahn, 2005; Raza et al., 2016), therefore possibly also contributing to better brain and mental health. These findings further expand the range of possible applications of RT interventions.

This review has several limitations. Firstly, it is based only on a small number of empirical studies. In addition, it is subject to the limitations of the individual studies, such as the small sample sizes per group, the lack of longitudinal studies or later follow-ups, and the correlational and often insignificant evidence. Another limitation is the individual differences in nutrition - diet was sometimes matched and documented but never manipulated. Additional limitations arise from comparing the studies. The studies used highly diverse subject pools as well as a variety of markers for antioxidants, oxidative stress, and oxidative damage which make it harder to compare the results, especially since particular markers (SOD, MDA) seem to react more reliably to RT than others (GSH, TAC, TNF-α). Yet, it can be seen as evidence for our conclusion that, despite the diversity in the compared studies, the positive effect could be consistently reported.

Future research should manipulate diet as a possible confounding factor and compare intensities over a wider spectrum to learn more about the dose-response relationship between RT and health. Longitudinal studies or later follow-ups should also be performed. To increase the comparability of studies, it would be helpful to have a standard of markers used to assess oxidative stress and damage as well as antioxidant capacity. Lastly, the mechanisms underlying the training adaptations of the redox systems should be investigated for a better understanding of the factors contributing to positive and possible negative effects.

To conclude, RT should be recommended as preventive and therapeutic health behavior to increase physical and mental health in the whole population. It is safe for all ages, genders, and personal backgrounds. Still, it is recommended to consult an expert to construct a training program that is adapted to individual characteristics and based on science to achieve optimal results.

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