

Moderate Intensity Training By Listening To Music Decreases Interleukin-6 Levels In Rats

Septyaningrum Putri Purwoto¹, Adi Pranoto², Hartono³ and Sugiharto^{3*}

¹STKIP PGRI Bangkalan, East Java, Indonesia

²Universitas Airlangga, Surabaya, East Java, Indonesia

³State University of Malang, East Java, Indonesia

sugiharto@um.ac.id

ABSTRACT

Decreasing levels of interleukin-6 (IL-6) is one of decrease inflammation indicators. This study aims to analyze the decrease of IL-6 serum levels in moderate and high intensity training by listening to music. The design of this study is the randomized control group posttest-only design, 21 of Rattus Norvegicus Strain Wistar male, 20-24 weeks, 250 ± 350 grams and randomly divided into 3 groups namely CONT (n = 7, control without treatment), MIT (n = 7, moderate intensity training, treadmill with speed 14-16 m/min for 15-30 minutes listening to music tempo 160 beats/min) and HIT (n = 7, high intensity training, treadmill with speed 22-25 m/min for 15-30 minutes listening to music tempo 160 beats/min). The intervention was started from 17.00-20.00 WIB with a frequency of 3 times / week for 10 weeks. Blood is drawn for 12 hours after the last training. Measurement of IL-6 serum levels using the ELISA method. Data analysis techniques using ANOVA test and LSD post hoc test with the Statistical Package for Social Science (SPSS). The results obtained IL-6 levels at CONT (1478,357 ± 495,209) pg / mL, MIT (850,500 ± 458,666) pg / mL, HIT (1756,928 ± 467,793) pg / mL and (p = 0.007). Based on the results of the study, it can be concluded that moderate intensity training by listening to music tempo 160 beats / min decreases IL-6 levels.

Keywords: Moderate Intensity Training, High Intensity Training, Fast Tempo Music, IL-6 Levels

Received December, 25, 2019; Revised January 24, 2020; Accepted February 15, 2020



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INTRODUCTION

Exercise is an interesting and enjoyable activity; it's not only have an impact on improving health, physical and physiological conditions, but also psychological (Sugiharto, 2012). In addition, exercise also has beneficial effects for the central nervous system (Ahmadiasl *et al.*, 2014), cardiovascular system (Mueller, 2007; Petersen and Pedersen, 2005), inhibits aging (Chung and Diffie, 2012) and prevents upper respiratory tract infection (URTI) (Nieman, 2012). Exercise effectively has a positive impact because exercise provides anti-inflammatory effects (Moynan *et al.*, 2013), treatment of chronic heart disease, diabetes mellitus type 2 and symptoms related to metabolic syndrome, so exercise is often used as an approach to improve and maintain physical as well as health (Lee and Paffenbarger, 2000; Kisan *et al.*, 2012). However, training also has an ambiguous nature which can have a negative impact (Sugiharto, 2012). This has not been widely understood by sports practitioners and the society.

Exercise has a dual function for the body, because exercise can be a stressor, which has the potential to cause distress, otherwise exercise can be also stimulator that can cause eustress (Sugiharto, 2012). It really depends on the dose of exercise that is done. Exercise that is done with the proper dose can be a stimulator for the body, while exercise with heavy and competitive doses can be a stressor for the body (Mastorakos *et al.*, 2005; Sugiharto, 2012). Stressors that occur in the body are not only physical stressors but also chemical, psychological and physiological stressors (Uchakin *et al.*, 2003), which are caused by heavy exercise doses. This is because heavy doses of exercise cause inflammation that is caused by muscle damage (Glesson, 2005). Inflammation is a stressor involving the Hypothalamic Pituitary Adrenal-axis (HPA-axis) and the immune system (Moynan *et al.*, 2013) which is characterized by cytokine secretion (Shaikh, 2011; Pedersen *et al.*, 2001). Cytokines are inflammatory mediators, such as tumor necrosis factor- α (TNF- α), interferon- γ (IFN- γ), interleukin-1 (IL-1), interleukin-6 (IL-6), radical oxygen and substances other pro-inflammatory found in blood circulation (Indra, 2007). IL-6 is an increased cytokine in response to exercise (Mohammadi *et al.*, 2012), IL-6 secretion precedes secretion from other cytokines (Febbraio and Pedersen, 2002; Petersen and Pedersen, 2006) and is a major cytokine that plays a central role in immune stimulation especially in inflammatory stress (Tsigos and Chrousos, 2002). Therefore, stress experienced must be managed properly; one method that is very effective and efficient in reducing stress is by listening to music (Sugiharto, 2009). This is because listening to music can increase enthusiasm during exercise so that it can improve health, fitness and achievement and the use of music consistently can reduce the occurrence of stress (Stefano, 2004). According to Chanda and Levitin (2013) explains that music is used to regulate mood and passion in everyday life and to improve physical and psychological health. Music is not just an auditive issue that is played through both ears, but it involves many aspects that are far more basic and profound (Djohan, 2010) and have the ability to capture attention, stimulate enthusiasm, produce emotions, change or regulate moods, evoke memories, enhance work output, reduce barriers and encourage rhythmic movements which all have potential applications in training (Terry and Karageorghis, 2006).

Research by Stefano *et al.* (2004) said that IL-6 levels decreased significantly due to Listening to music, but when exercise caused an increase in proinflammatory cytokines TNF- α and IL-1 β and caused a dramatic increase in responsive inflammation of the IL-6 cytokine responsiveness if performed with heavy doses (Ostrowski *et al.*, 1999). Likewise

in the research of Zhang *et al.* (2007) that IL-6 increased due to heavy exercise dose, not only that the Bruce test exercise caused a significant increase in serum IL-6 and IL-33 levels after training compared to before training in volleyball athletes (Ali, 2014), during training 30 minutes with an intensity of 65% -70% of maximal oxygen uptake (VO₂max) also significantly increased IL-6 levels (Mohammadi, 2011), moderate exercise for 45 minutes with an intensity of 50% VO₂max increased IL-6 levels (Shojaei *et al.*, 2011), exercise for 12 months reduces levels of IL-6 (Oberbach, 2008). Other researchers found an increase in IL-6 levels after 2 hours of eccentric training, but did not occur in concentric exercises (Bruunsgaard *et al.*, 1997). Lyngso (2002) found the same thing with moderate exercise for 60 minutes, heavy doses of exercise caused an increase in proinflammatory cytokines TNF- α and IL-1 β and caused a dramatic increase in inflammatory responsive cytokine IL-6 (Ostrowski *et al.*, 1999) On the contrary, moderate-dose exercise can significantly reduce IL-6 (Starkweather, 2007). Based on the background of the problem above, the purpose of this study is to analyze the decrease in serum IL-6 levels in moderate and high intensity exercise by listening to music.

METHODS

Research design

The design of this study is the randomized control group posttest-only design, 21 of Rattus Norvegicus Strain Wistar male, 20-24 weeks, 250 \pm 350 grams and randomly divided into 3 groups namely CONT (n = 7, control without treatment), MIT (n = 7, moderate intensity training, treadmill with speed 14-16 m / min for 15-30 minutes listening to music tempo 160 beats / min) and HIT (n = 7, high intensity training, treadmill with speed 22-25 m / min for 15-30 minutes listening to music tempo 160 beats / min).

Exercise Protocol

Moderate intensity exercise is done by rats running on a treadmill with a speed of 14-16 m / min for 15-30 minutes by listening to music tempo 160 beats / min whereas, high intensity exercise with a speed of 22-25 m / min for 15-30 minutes by listening to music tempo 160 beats / min. The intervention was carried out at 17.00-20.00 WIB with a frequency of 3 times / week for 10 weeks.

Blood analysis

Blood is drawn from the left ventricle of experimental animals as much as 5 ml. Blood drawn 12 hours after the last exercise. Measurement of IL-6 levels using ELISA kit (Catalog No. E-EL-R0015; Elabscience, Inc., China, 2018) with a unit of concentration of pg / mL.

Statistical Analysis

Statistical analysis is using packet statistics for social science (SPSS) software (Chicago, IL, USA). The normality test uses the Shapiro-Wilk test, while the homogeneity test uses the Levene test. Data that are normally distributed and have a homogeneous variant are tested using the ANOVA test and continued with the post hoc LSD test with a significant level (p <0.01). All data are displayed with mean \pm SD.

RESULTS

The results of data analysis of average IL-6 levels after MIT and HIT intervention for 10 weeks can be seen in table 1.

Table 1. Average IL-6 levels after MIT and HIT intervention

Kelompok	N	Mean±SD (pg/mL)	ANOVA p-values
CONT	7	1478.357±495.209 ^a	0.007*
MIT	7	850.500±458.666 ^b	
HIT	7	1756.928±467.793 ^a	

Note: Different superscripts indicate that there are significant differences in the LSD post hoc test with ($p < 0.01$).

Based on table 1 it can be seen that the IL-6 level at MIT is lower than that of HIT and CONT. Based on ANOVA test results showed that there were significant differences in the average levels of IL-6 ($p = 0.007$). Based on the LSD post hoc test, there was a significant difference in IL-6 levels between MIT and CONT ($p = 0.023$), MIT and HIT ($p = 0.002$), while HIT with CONT were no significant differences ($p = 0.286$), but based on the value the average IL-6 level in HIT tends to be higher than the average CONT value.

DISCUSSION

This study aims to analyze the decrease in serum IL-6 levels in moderate and high intensity training by listening to music. The novelty of our method is the use of music tempo 160 beats/ min. To meet these objectives, we combine moderate and high intensity exercise with listening to music tempo 160 beats / min. Based on the results of the study, it is showed that IL-6 levels at MIT were lower than those of HIT and CONT.

Based on the results of the study, it is showed that there were significant differences in IL-6 levels between MIT and CONT ($p = 0.023$). These results are in line with the results of a study conducted by Stefano *et al.* (2004) concluded that IL-6 levels decreased significantly after listening to music, as well as after moderate-intensity training for 12 months significantly reduced IL-6 levels (Oberbach, 2008). Research conducted by (Starkweather, 2007) found similar results that moderate intensity exercise lowers IL-6 levels. However, these results are different from the study results that are conducted by Markovitch *et al.* (2008) he is concluded that IL-6 levels increased significantly after doing moderate intensity exercise. This study conducted by Mohammadi (2011) found similar results those 30 minutes of exercise with an intensity of 65% -70% VO₂max also significantly increased IL-6 levels. This difference caused by the use of music tempo 160 beats / min for this study, whereas in previous studies did not use music. This is possible because the use of music tempo 160 beats / min in this study affects the decrease in IL-6 levels. According to the results of research conducted by Okada (2008) concluded that exercise by listening to music reduces levels of IL-6. The combination of exercise with music can affect the body's physiology, this is because various musical features, namely rhythm, tempo and genre can increase energy tolerance through distraction and increase comfort (Savitha *et al.*, 2013) and reduce muscle fatigue during exercise (Bakhtiar *et al.*, 2012). In addition, exercise by listening to music can also reduce stress responses which are marked by a decrease in cortisol secretion (Sugiharto, 2009). Decreased cortisol secretion will reduce the secretion of IL-6 (Daloi *et al.*, 2014), so that moderate intensity exercise by listening to music can be a stimulator for the body which has the potential to cause anti-inflammatory effects for the body (Moylan *et al.*, 2013) which has an impact on increasing

the quality of physical, psychological and health conditions (Sugiharto, 2009; Sugiharto, 2012).

There was a significant difference in IL-6 levels between MIT and HIT ($p = 0.002$). This difference is due to the treatment of MIT and HIT. Although MIT and HIT were given the same music, the influence of MIT and HIT gave different responses to IL-6 levels. According to Neto *et al.* (2016) that exercise is a strategy in reducing the inflammatory process. In addition, exercise is also considered as stressor. If exercise is considered as stressor, the body will react by increasing awareness of threats that can interfere with homeostasis. The threat signal will be responded by the body with the mechanism of general adaptation syndrome or GAS (Sugiharto, 2012), but exercise is also considered a stimulator. According to (Mastorakos & Pavlatou, 2005) HIT becomes a stressor for the body, otherwise exercise as a stimulator when it is done with MIT. This is likely due to the MIT coping mechanism. The coping mechanism is the body's effort to fight the pressure, so that it gradually adapts to stress, so that it feels "good" in the face of shock, then a higher adaptation occurs (Rushall & Pyke in Sugiharto, 2012). At MIT, cortisol secretes to make adaptation mechanisms to stress (Sugiharto, 2012), with the result that cortisol secretion is lower which triggers a decrease in IL-6 (Daloii *et al.*, 2014). This is similar to previous study conducted by (Sugiharto, 2009) that listening to music in submaximal intensity exercises tends to decrease cortisol secretion. So MIT can be a stimulator for the body (Sugiharto, 2012).

ANOVA test results (Table 1) showed that there was no significant difference in IL-6 levels between HIT and CONT ($p = 0.286$). However, when it is viewed from the average value of HIT, it tends to have higher IL-6 levels compared to CONT. These results are in line with the results of a study conducted by Eaton *et al.* (2018) concluded that high-intensity interval training (HIIT) caused an increase in IL-6 levels of ~ 25-fold and 3 hours after the intervention there was an increase of ~ 30-fold. High levels of IL-6 in HIT may be caused by increased contraction of a muscle during exercise. Because when there is muscle contraction during exercise there is an increase in energy demand, causing the muscles to work harder in supplying energy (Melinda, 2004). Meeting energy needs during exercise can increase muscle contraction which is characterized by increased IL-6 secretion. Muscle secreted IL-6 helps maintain metabolic homeostasis (Febbraio and Pedersen, 2002) which play a role in regulating metabolism in adipose tissue, skeletal muscle and liver (Lutoslawska, 2012). Adipose and liver tissue contribute to maintain glucose homeostasis, inducing lipolysis and inhibiting the effects of pro-inflammatory cytokines such as TNF- α , thus protecting against insulin resistance and atherosclerosis (Pedersen *et al.*, 2001). During exercise will increase the consumption of muscle substrate and increase glycogen and fat oxidation, thereby activating lipolysis in adipose tissue (Yazdani *et al.*, 2013). Lipolysis activates in fat tissue to provide energy to muscles, but also has a positive effect on intramuscular fat utilization. According to Lutoslawska (2012) IL-6 also stimulates cell satellite and muscle hypertrophy and muscle repair, because it is an important molecule of muscle hypertrophy by controlling cell satellite proliferation and myonuclear accretion mediated by the activation of signal transducers and activators of transcription 3 (STAT3) (Serrano *et al.*, 2008), glycogen synthesis through phosphatidylinositol-3 kinase (PI3K) (Al-Khalili *et al.*, 2006). In addition, IL-6 can also affect lipid metabolism (Pedersen and Febbraio, 2005) through the mechanism of mitogen-activated protein kinase (MAPK) in skeletal muscle (Al-Khalili *et al.*, 2006). High levels of IL-6 in HIT may also occur due to a mechanism between the muscles and the brain.

According to Pedersen and Febbraio (2005) IL-6 connects the mechanism for direct interaction between muscle and brain, so it has a lot of effects on brain function, IL-6 also crosses the blood brain barrier so that it not only affects metabolism during exercise, but also regulates muscle activity, affects mood, performance and cognitive function. On the other hand, high levels of IL-6 in HIT may be caused by stress levels experienced. Stress affects the activation of the Hypothalamus-Pituitary-Adrenal axis (HPA-axis) axis (Clark and Mach, 2016), which its functions to stimulate an increase in Corticotrophin-Releasing Hormone (CRH) (Sugiharto, 2012) and secrete the hormone Adenocortico-tropin Hormone (ACTH) (Powers and Howley, 2015). ACTH secretion stimulates the secretion of the hormone cortisol (Usui *et al.*, 2011). Cortisol causes an increase in cytokine secretion (Walsh *et al.*, 2011), as an inflammatory mediator (Indra, 2007). One of the inflammatory mediator cytokines is IL-6. IL-6 is a major endocrine cytokine that has a major role in immune stimulation, especially in inflammatory stress (Tsigos and Chrousos, 2002).

CONCLUSION

Moderate intensity training by listening to music tempo 160 bpm / min significantly decreases IL-6 levels. Moderate intensity training with listening to music tempo 160 bpm / min and performed it for 15-30 minutes with a frequency of 3 times / week for 10 weeks has a positive effect in reducing inflammation compared with high intensity training and control. Based on the results of the study it is recommended to do further research by adding several other parameters such as tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), interleukin-1 α (IL-1 α) and interleukin-8 (IL-8) as an indicator of proinflammation, while interleukin-1 (IL-1), interleukin-1ra (IL-1ra) and interleukin-10 (IL-10) as indicators of anti-inflammatory, cortisol, blood glucose and muscle protein.

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