# THE DUAL BENEFITS OF HIGH-INTENSITY INTERVAL TRAINING: IMPROVING COGNITION AND REDUCING BODY WEIGHT IN SCHIZOPHRENIA PATIENTS ON RISPERIDONE

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### **ABSTRACT**

This quasi-experimental study investigated the effects of High-Intensity Interval Training (HIIT) on weight loss and cognitive function in patients with schizophrenia treated with risperidone. Conducted at Dadi Regional Special Hospital, South Sulawesi, Indonesia, the study included 40 participants who met the inclusion criteria, including males aged 20–40 years, with disease onset of fewer than five years, and receiving risperidone therapy (4–6 mg/day). The exclusion criteria included severe organic comorbidities and recent substance use. The participants were divided into treatment and control groups, with the former undergoing 30 HIIT sessions over 10 weeks. Each session lasted 25 min, incorporating warm-up, core HIIT, and cool-down phases, with heart rates monitored to ensure anaerobic intensity (80–90% of maximum heart rate). The results showed a significant weight reduction in the treatment group (mean decrease:  $0.475 \, \text{kg}$ , p < 0.001), indicating the potential of HIIT to mitigate risperidone-induced weight gain. Cognitive performance, assessed via the Schizophrenia Cognitive Rating Scale (SCoRS v BI), improved in both groups, with no significant differences between them (p > 0.05). However, greater improvement was observed in the treatment group. This study supports the integration of HIIT as adjunct therapy for schizophrenia, offering the dual benefits of cognitive enhancement and weight management. Further research incorporating genetic factors and advanced monitoring tools is needed to refine these findings.

Keywords: body weight, cognitive function, physical exercise, risperidone, schizophrenia

# INTRODUCTION

According to the National Alliance on Mental Illness (2022), Schizophrenia is a chronic mental health disorder characterized by disruptions in cognition, emotions, and behavior. National Alliance on Mental Illness (2022) and National Institute of Mental Health (2022) classify the manifestations of schizophrenia as either positive or negative, with cognitive being the third primary category. However, these manifestations might vary from person to person. According to the World Health Organization (WHO), Approximately 24 million people globally suffer from schizophrenia. (WHO, 2022). The prevalence of schizophrenia in Indonesia increased from 1.7% per thousand in 2013 to 7% per thousand in 2018, according to statistics from Basic Health Research (Riskesdas) in 2018. When considering the prevalence of schizophrenia within Indonesia, it is worth noting that South Sulawesi Province ranks sixth highest. According to Kemenkes (2018), the incidence rose from 1.8% per mile in 2013 to 9% per mile in 2018.

Cognitive performance associated with schizophrenia has been found to deteriorate, and negative symptoms worsen when firstgeneration antipsychotics are administered. Second-generation antipsychotics (APG-2) and atypical antipsychotics, such as risperidone, should be considered because of their effects on both D2 and 5 dopamine receptors. In terms of cognitive performance and the amelioration of both positive and negative symptoms, -HT2A's strong affinity for alpha 1 and alpha 2 adrenergic receptors is a major advantage (Kusumawardhani et al, 2011). The gold standard for schizophrenia care is a combination of pharmaceutical and non-pharmacological treatments, because it outperforms any approach alone (Kusumawardhani et al., 2011).

The Schizophrenia Cognitive Rating Scale (SCoRS) serves as a measurement tool derived from interviews, emphasizing the assessment of daily functioning. The SCoRS comprises 20 question items that the interviewer is required to pose to both the patient and informant during distinct interviews. Informants are individuals who maintain relationships and engage in numerous daily interactions with their patients. Potential informants may include relatives, acquaintances, social workers, and healthcare professionals. Each item was evaluated using a four-point measurement scale, which included 1 = none, 2 = light, 3 = medium, and 4 = severe. Additionally, one may consider the option of incorporating an N/A (nonapplicable) scale. There may be reasons why this question cannot be applied to the patient's situation (Keefe et al., 2006). The interviewer was also required at the end of the interview to fill out a global functional scale evaluation (ranging from 1 to 10), in addition to the 20-question questions. A score of 1 indicates no cognitive dysfunction and a score of 10 indicates the most severe level of cognitive impairment; this comprehensive functional scale evaluation is used to determine whether individuals diagnosed with schizophrenia have cognitive impairment (Keefe et al, 2006).

Herdaetha and Raharjo (2008) validated the Indonesian iteration of SCoRS (SCoRS vs. BI), which resulted in the following findings. Upon assessing the validity of the questions posed to the patient, it is evident that six questions, which account for 30% of the total, had a high validity value. Conversely, 14 questions, which account for 70% of the total, had a very high validity value. The SCoRS v BI instrument exhibited a high level of reliability, as evidenced by a reliability coefficient of 0.976, as represented by Cronbach's alpha. Upon assessing the validity of each inquiry posed to the informant, it was evident that seven questions (35%) exhibited a high validity value, whereas 13 questions (65%) demonstrated a very high validity value. The reliability coefficient, as denoted by Cronbach's alpha, was 0.977, indicating a high level of reliability of the SCoRS v BI instrument. The sensitivity and specificity assessments yielded significantly higher values, with a sensitivity of 92.8% and a specificity of 93.7%, respectively. This indicates that The SCoRS v BI tool is reliable for measuring cognitive function with a high reliability score (Rahardjo et al, 2008).

Exercise therapy is a non-pharmacological tactic that has been suggested as a potential adjunct to pharmaceutical treatments. The positive effects of exercise on the treatment of schizophrenia and other mental health conditions have been demonstrated in a large body of research. Improvements include lessening both good and bad symptoms, improvement of cognitive function, and enhancement of the general quality of life. Exercising the hippocampus improves brain plasticity in people with schizophrenia, according to studies. This means that people with schizophrenia may benefit from including exercise in their treatment plan (Girdler et al., 2019).

Although traditional aerobic exercise is frequently advocated for the improvement of cardiovascular health, it may pose difficulties for individuals with schizophrenia, attributable to factors such as diminished motivation or physical constraints. High-intensity interval training (HIIT) is a more effective option, necessitating reduced time commitments and elevated intensities to attain benefits comparable, if not superior, to those derived from prolonged aerobic exercise (Girdler et al, 2008). Moreover, the rigorous characteristics of HIIT may enhance motivation and satisfaction in individuals with schizophrenia, consequently fostering greater adherence to exercise routines.

This study aimed to explore the combined impact of high-intensity interval training (HIIT) and risperidone therapy on both the physical and psychological health of individuals diagnosed with schizophrenia. We propose that HIIT could potentially promote the synthesis of nerve growth factor (NGF) and diminish systemic inflammation, thereby improving cognitive function, which is often compromised in this demographic. Moreover, weight reduction achieved through high-intensity interval training could enhance the overall quality of life and foster greater adherence to treatment among those diagnosed with schizophrenia.

The urgency of measuring body weight is underscored by its significant implications for health management, particularly in patients undergoing treatments that can alter their body

composition, such as antipsychotic medications. Risperidone patients often experience weight gain, which necessitates regular monitoring of body weight to mitigate the associated health risks (Oka et al., 2010; Bardazzi et al., 2010). Furthermore, the implementation of high-intensity interval training (HIIT) has been shown to effectively reduces body weight and improves muscle mass, thereby counteracting the adverse effects of medication-induced weight gain (Højman et al., 2014; Ali, 2014). This dual approach addresses the physical aspects of health and enhances cognitive function, making it a comprehensive strategy for managing the overall well-being of patients with schizophrenia (Dowthwaite et al., 2014; Mrowietz et al., 2010). Therefore, integrating regular weight assessments with targeted exercise interventions is crucial for optimizing the health outcomes in this population. The results of this study are anticipated to offer empirical support for the advancement of more cohesive, exercise-oriented interventions in the treatment of schizophrenia.

### **METHODS**

The classification of this investigation employed a quasi-experimental design, utilizing pre- and post-tests alongside random group selection, whereby variables were assessed before and after the intervention. Additionally, this study employed a single-blind methodology. The investigation was conducted at the Dadi Regional Special Hospital (RSKD) located in the province of South Sulawesi. The study population consisted of patients with schizophrenia treated at the Dadi Special Regional Hospital in South Sulawesi Province. The sample for this study included all patients with schizophrenia in the stable phase who were treated at the Dadi Special Regional Hospital in South Sulawesi Province, met the inclusion criteria, and did not meet the exclusion criteria.

The study subjects were divided into two groups: the Control Group (patients who met the inclusion criteria but did not receive exercise therapy sessions) and the Treatment Group (patients who met the inclusion criteria and received exercise therapy sessions for 10 weeks, equivalent to 30 sessions).

The sampling technique for each group was performed using Consecutive Sampling, which meant that all patients met the selection criteria. The inclusion criteria were as follows: patients diagnosed with schizophrenia according to PPDGJ III, male aged 20-40 years, patients with a disease onset of less than 5 years, patients who have passed the acute phase (PANSS-EC < 15), able and willing to participate in exercise therapy sessions, agree to the informed consent for the study, and receive risperidone therapy of 4-6 mg/day. The exclusion criteria included severe organic comorbidities and a history of substance use (narcotics, psychotropics, and addictive substances) within less than one year before being admitted to the hospital. The dropout criteria were irregular participation in exercise sessions (<80% attendance), the subject's heart rate not reaching optimal levels (Zone 4: anaerobic zone 80-90% of the maximum heart rate during several exercise sessions), irregular use of risperidone, refusal to continue the study, and passed away.

Informed permission forms, the SCoRS v BI scale, PANS-EC scale, risperidone, and exercise training equipment (a sound system and an LCD) were all part of the study's instrumentation.

Each patient who met the criteria for schizophrenia according to DSM-V and PPDGJ III and met the inclusion criteria while not falling under the exclusion criteria for the research group was recorded and underwent a medical history interview. The researcher then explained the purpose and objectives of the study to the families and research subjects. If they agreed, they were included in the study (informed consent). The research subjects were divided into two groups: control and treatment. The treatment group was given exercise therapy sessions with the following conditions: 1) the exercise was in the form of High Intensity Interval Training (HIIT) or interval training; 2) each session lasted 25 minutes; 3) the first and last 5 minutes were used for warm-up, while the remaining 15 minutes were dedicated to the core interval training movements; 4) the exercise sessions were performed with moderate to high intensity; 5) heart rate measurements were taken before, at the midpoint, and at the end of each session; 6) SCoRS v BI scores were assessed for both groups at baseline, week 5, and week 10.

The interviewer was obligated to ask the patient, and the informant separated sets of questions from the ScoRS v BI, which consisted of 20 independent items. On a scale of 1 (none)

to 4 (severe), each question item was assessed using a four-point measuring system. In addition, an N/A (non-applicable) scale is an alternative. It would be reasonable to assume that this issue is irrelevant given the patient's state. At the end of the interview, in addition to the 20 questions, the interviewer must also complete a global functional scale evaluation (with a range of 1 to 10). Scoring from 1 (no cognitive dysfunction) to 10 (severe cognitive impairment), this global functional assessment was designed to determine whether individuals diagnosed with schizophrenia had cognitive dysfunction.

Ethical approval was obtained from the Biomedical Research Ethics Commission on Humans, Faculty of Medicine, Hasanuddin University, and consent was obtained from both participants and their families. The investigator ensured that informed consent was obtained prior to the subject's participation in the study while also striving to uphold the confidentiality of the research subject's identity.

The independent variable pertains to the specific treatment modality, which is characterized by physical exercise training, specifically high-intensity interval training (HIIT). The variable that is contingent upon other factors is SCoRS versus BI Score. Moderating variables included age, body weight before and after treatment within the treatment group, sex, educational background, onset of disease, use of atypical antipsychotics, smoking habits, genetic predisposition, and personality traits.

Following documentation of the study instruments, data analysis was conducted using SPSS 25.0. The Mann-Whitney U test was used to compare the treatment and control groups for data that did not conform to a normal distribution. An Independent T-test was used when the data exhibited a normal distribution. The Wilcoxon test is applicable when data distribution deviates from normality, whereas the Paired T test is suitable for normally distributed data. These tests assessed changes within the groups before and after treatment. In cases of normal data distribution, Pearson's test was employed to assess correlations. Spearman's test was used when data distribution deviated from normality. A p-value below 0.05 indicates that the statistical test results are deemed significant. The processed data are presented in both numerical and categorical forms. Numerical data are expressed as the median (lowest, highest) or mean  $\pm$  standard deviation. The proportions serve as a method for expressing categorical data.

# RESULTS AND DISCUSSIONS

Table 1 demonstrates that the treatment group had 9 individuals (45%) with high school education, whereas the control group contained 11 individuals (55%). The junior high school treatment group consisted of seven individuals, accounting for 35%, whereas the control group had four individuals, representing 20%. At the elementary level, the treatment group comprised four persons (20%), whereas the control group consisted of five individuals (25%).

The attributes of the balanced treatment group indicated an even distribution, with 10 individuals (50%) participating in work and 10 persons (50%) not participating in work. In the control group, 12 (60%) were employed, whereas 8 individuals, comprising 40%) were unemployed. In the therapy group, marital status indicated that 12 individuals (60%) were married, whereas eight individuals (40%) were unmarried. In the control group, 11 individuals (55%) were married, whereas 9 individuals (45%) were unmarried. In the therapy group, illness onset was uniformly distributed, with 10 individuals (50%) having onset in less than 1 year and 10 persons (50%) reporting onset in over 1 year. In the control group, 13 patients (65%)

**Table 1.** Demographic Characteristics of Research Subjects (N=40)

Characteristics	Total (N=40)	Treatment (n=20)	Control (n=20)	p
	%	%	%	-
Education				
Elementary	9 (22.5)	4 (20.0)	5 (25.0)	2.
Junior HS	11 (27.7)	7 (35.0)	4 (20.0)	2
Senior HS	29 (50.0)	9 (45.0)	11 (55.0)	
Employment				
Employed	22 (55.0)	10 (50.0)	12 (60.0)	0.379
Unemployed	18 (45.0)	10 (50.0)	8 (40.0)	
Marital Status				
Married	23 (57.5)	12 (60.0)	11 (55.0)	0.555
Not Married	17 (42.5)	8 (40.0)	9 (45.0)	
Disease Onset				
< 1 year	23 (57.5)	10 (50.0)	13 (65.0)	0.179
>= 1 year	17 (42.5)	10 (50.0)	7 (35.0)	

exhibited symptom onset within one year, whereas seven individuals (35%) reported onset after more than one year.

The distribution of the research subject data exhibited notable differences between the treatment and control groups. Upon conducting the homogeneity test, it was observed that the p-value for all variables exceeded 0.05 (p>0.05). This confirmed that the participants in this study exhibited homogeneity and were suitable for subsequent analytical evaluations.

The information presented in Table 2 and Figure 1 illustrates a noteworthy decrease in weight after an exercise regimen exceeding two months within the treatment group, as indicated by a p-value of 0.001 (<0.05).

Table 3 illustrates the methodology for monitoring the treatment group engaged in physical exercise training through High-Intensity Interval Training (HIIT). Historically, it has been essential to ascertain the maximum heart rate (DJM), calculated as 220 minus one's age. Subsequently, we determined the heart rate corresponding to each respondent's anaerobic zone, defined as 85% DJM. Each individual had a unique anaerobic zone. The table presents the average values of all participants engaged in physical exercise training within the anaerobic zone calculated based on the number of individuals

Table 2. Body Weight Before and After Treatment

<b>Body weight</b>	Mean±	p
Initial BW	55.800	
Final BW	55.325	0.0001
Initial BW-Final BW	$0.475 \pm$	

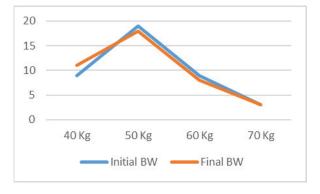


Figure 1. Body Weigt Before and After
Treatment

**Table 3.** Heart Rate Monitor of the Treatment Group

Treatment	Age	Maximum Heart Rate (220-Age)	Zone 4 (80- 90% DJM Anaerobik)	Mean	Min-Max
Sampel	40	180	144-162	151,8667	146-158
Sampel	28	192	154-173	154,8667	150-160
Sampel	43	177	142-159	151,6	142-156
Sampel	38	182	146-174	152,1333	146-158
Sampel	27	193	154-174	154,8667	152-158
Sampel	33	187	150-168	152,8667	150-158
Sampel	26	194	155-175	155,8	148-160
Sampel	24	196	157-176	155,2667	150-160
Sampel	28	192	154-173	155,1333	150-160
Sampel	33	187	150-168	154	150-160
Sampel	34	186	149-167	154,2667	152-160
Sampel	42	178	142-160	152	144-156
Sampel	25	195	156-175	155,4667	150-160
Sampel	38	182	146-174	153,7333	148-160
Sampel	36	184	147-166	153,8	148-158
Sampel	32	188	150-169	154,2	150-158
Sampel	39	181	149-163	154,8	150-158
Sampel	44	176	141-158	153	148-158
Sampel	45	175	140-158	151,3333	144-158
Sampel	41	179	143-161	152,4667	146-160

involved. This indicates that, according to the heart rate measurements, each participant classified themselves within the high-intensity category during their physical exercise training.

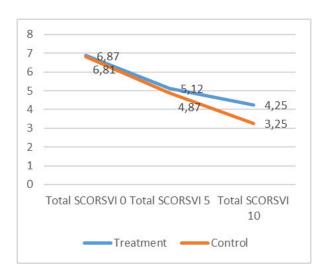
Prior to conducting a comparative analysis of SCoRS versus BI values across each group at baseline, the 5th week, and the 10th week (session 30), a normality test was initially performed using the Shapiro-Wilk test because the sample size was less than 50. A normality test indicated that the data were not normally distributed. Consequently, to compare the SCoRS and BI scales by group, the Mann-Whitney test was employed, with the results presented in Table 4 and Figure 1.

Table 4 presents a comparative analysis of cognitive function across different groups. The p-value was derived from the comparison of variations in the SCoRS vs. BI score between the treatment and control groups (p > 0.05). From a statistical perspective, the changes observed in the SCoRS v BI scores between the two groups did not exhibit any significant differences.

A normality assessment was conducted using the Shapiro-Wilk test. The normality test revealed

Table 4.	Comparison of Cognitive Function by Group
	(Mann-Whitney test)

Variable	Group	N	Median (Min-Max)	SD	p
Total ScorS v BI (Baseline)	Treatment	20	6.87 (3.75-10.0)	1.17	0.914
	Control	20	6.81 (3.50-8.37)	1.68	0.914
Total ScorS v BI (5 <sup>th</sup> week)	Treatment	20	5.12 (2.75-7.12)	0.81	0.488
	Control	20	4.87 (3.62-6.12)	1.00	
Total ScorS v BI (10 <sup>th</sup> week)	Treatment	20	4.25 (2.25-5.75)	1.01	0.287
	Control	20	3.25 (2.50-5.37)	1.02	0.207



**Figure 2.** Comparison of Cognitive Function

the presence of data that deviated from normal distribution. Consequently, to compare the SCoRS and BI scales, the Wilcoxon signed-rank test was used (see Table 5).

Table 5 provides a comparative analysis of cognitive functions over the weeks. In the treatment group, significant results were observed, particularly a reduction in the median total SCoRS v BI (baseline–5th week), which declined from 6.87 to 5.12 (p <0.001). A notable decrease in the median total SCoRS v BI was recorded from baseline to the 10th week, declining from 6.87 to 4.25 (<0.001). A notable decrease in the median total SCoRS v BI was recorded from the 5th week to the 10th week, declining from 5.12 to 4.25 (p < 0.001). A significant decrease in the median

total SCoRS v BI (baseline-5th week) was noted in the control group, with values declining from 6.81 to 4.87 (p <0.01). A significant decrease was noted in the median total SCoRS vs. BI (baseline – 10th week), from 6.81 3.25 (<0.001). A significant decrease in the median total SCoRS v BI was recorded from the 5th week to the 10th week, declining from 4.87 to 3.25 (p < 0.001). Several underlying factors contribute to this issue, including fatigue, the effects of antipsychotic medications, metabolic and cardiorespiratory health concerns, diminished motivation for physical exercise, potential links to the disorder's negative symptoms, and insufficient resources or support from others to promote increased daily physical engagement (Viljoen & Roos, 2020).

Therefore, it is important to integrate non-pharmacological therapies with daily pharmaceutical treatments. Physical exercise is an adjunctive treatment modality. Participation in physical activity and training serves as a beneficial supplementary method to improve cognitive performance in patients (Vilijoen & Roos, 2020; Girdler et al., 2019). This relates to a particular area of the brain, the hippocampus, which is essential for learning and memory processes (Girdler et al, 2019).

Numerous foundational elements are identifiable, including fatigue, the effects of antipsychotic medications, metabolic and cardiorespiratory health issues, diminished motivation for physical activity (potentially linked to the disorder's adverse symptoms), and insufficient resources or support for engaging in activities that promote regular physical engagement (Viljoen & Roos, 2020). Integrating non-pharmacological interventions with daily pharmacological therapies is essential. Physical exercise is an important supplementary method for therapeutic intervention. Engaging in physical exercise and training is an advantageous adjunct that may enhance cognitive function in patients (Vilijoen & Roos, 2020; Girdler et al., 2019). The hippocampus is a region of the brain that

are crucial for learning and memory (Girdler et al, 2019).

Neuronal atrophy likely accounts for the smaller hippocampal volume seen in patients with schizophrenia compared to the general population,

Group	Variable	n	Median	SD	p
			(Min-Max)		
Treatment	Total SCoRS v BI (Baseline)	20	6.87 (3.75–10.00)	1.17	0.000
	Total SCoRS v BI (5th week)	20	5.12 (2.75–7.12)	0.81	
	Total SCoRS v BI (Baseline)	20	6.87 (3.75–10.00)	1.17	0.000
	Total SCoRS v BI (10th week)	20	4.25 (2.25–5.75)	1.01	
	Total SCoRS v BI (5th week)	20	5.12 (2.75–7.12)	0.81	0.000
	Total SCoRS v BI (10th week)	20	4.25 (2.25–5.75)	1.01	
Control	Total SCoRS v BI (Baseline)	20	6.81 (3.51–8.37)	1.68	0.002
	Total SCoRS v BI (5th week)	20	4.87 (3.62–6.12)	1.00	
	Total SCoRS v BI (Baseline)	20	6.81 (3.50–8.37)	1.68	0.000
	Total SCoRS v BI (10th week)	20	3.25 (2.50–5.37)	1.01	

**Table 5.** Cognitive Function by Week (Wilson Signed Rank Test)

according to previous studies. According to Girdler et al. (2019), individuals with schizophrenia may have difficulties in memory, cognition, and executive functioning if there are abnormalities in the hippocampus. Exercise regularly improves executive function, memory, processing speed, attention, and processing in patients with schizophrenia. Cognitive enhancement is facilitated by exercise training because it improves blood flow and volume to the hippocampus, promotes neurogenesis, influences synaptic plasticity, and elevates the levels of growth factors, such as BDNF. This plays an essential role in reducing cognition.

Memory and hippocampal and neural plasticity impairments (Girdler et al., 2019).

Researchers in this study measured participants' cognitive capacity changes using.

The SCoRS v BI scale was validated in 2008. Rahardjo et al. (2008) found that when the SCorSv BI score decreased, it signified an improvement in cognitive function. High-Intensity Interval Training (HIIT) was used in 30 sessions, each lasting 25 minutes, to increase the activity that the research participants did. Compared to conventional exercise, which mostly involves lowto moderate-intensity aerobic zones, HIIT takes a very different approach. The maximum heart rate was originally assessed in all treatment groups using 220-Age calculation in this investigation. We then calculated the anaerobic zone heart rates for each participant, which are 80-90% of the DJM. The age difference among the respondents was likely responsible for the observed variations in their anaerobic zones. In line with recent research,

which indicated that peak lactate levels are often during high-intensity interval training (HIIT) at a heart rate (HR) of approximately 85%. Maximum HR, the anaerobic zone, has been identified (Andrews et al., 2020; Weaver et al., 2021). The role of lactate in enhancing brain plasticity has been the subject of several scholarly studies. The physiological benefits of high-intensity exercise may be comparable to or greater than those of conventional mild-to-moderate intensity exercise, according to a number of prior clinical studies. The results showing less cortical inhibition and higher excitability in the motor cortex suggest that HIIT may be a more efficient way to improve plasticity in this region of the brain (Weaver et al., 2021).

High-Intensity Interval Training (HIIT) has been shown to mitigate the weight gain associated with risperidone treatment in patients with schizophrenia. Risperidone, an atypical antipsychotic, induces weight gain through mechanisms involving the hypothalamic arcuate nucleus and serotonin receptors, particularly the 5-HT2C receptor, which stimulates appetite and food intake (Wan et al., 2019; Li et al., 2021). Studies indicate that patients receiving risperidone often experience metabolic disturbances, including increased body mass index (BMI) and insulin resistance (Alan & Kültür, 2013; Soe, 2024).

The integration of HIIT into treatment regimens for these patients has demonstrated benefits, potentially enhancing cognitive function while promoting weight loss (Kong et al., 2017; Liu et al., 2022). Research indicates that HIIT can counteract the metabolic side effects of

antipsychotics by improving insulin sensitivity and reducing fat mass (Qiu et al., 2023; Libowitz & Nurmi, 2021). This approach not only addresses the physical health concerns associated with risperidone, but also supports overall mental health outcomes, making it a valuable component of comprehensive care for individuals with schizophrenia (Chen et al., 2019; Cooper et al., 2016).

Both the treatment and control groups exhibited enhancements in cognitive function, as indicated by a decrease in the SCoRS vs. BI score. The research indicated no statistically significant difference in the reduction of the SCoRS vs. BI score between the two groups. Compared to the control group, the treatment group exhibited a more favorable trend in decreasing the total SCoRS vs. BI score. Risperidone, an atypical antipsychotic, has demonstrated efficacy in reducing both the positive and negative symptoms of schizophrenia, as well as in delaying cognitive decline. This may account for the observed decrease in SCoRS vs. BI scores in the control group. Risperidone significantly inhibits both the D2 and 5HT2A receptors in glutamate neurons within the brain (Stahl, 2013; Stepnicki et al., 2018), making this a critical factor to consider. The lack of significant variation in cognitive function improvement between the treatment and control groups can be attributed to several factors. The unique genetic predisposition of individuals is likely to contribute to this phenomenon. Multiple genetic variations are recognized as possible risk factors for schizophrenia. Variations in the COMT (catechol O-methyltransferase) gene, DTNBP1 (dystrobrevin binding protein 1) gene, and NRG1 SNP1 and SNP2 (neuregulin-1 single nucleotide polymorphism 1 and 2) genes were noted (Sutrisna & Aisyah, 2010). The expression of various genes in distinct brain regions such as the hippocampus and cerebral cortex has been implicated in numerous polymorphisms (Owen et al., 2004). Weaver et al., Andrews et al., and Griffijoyo and Sidik (2013) did not examine their influence on cognitive performance.

This study has various limitations, including the dependence on PPDGJ III for diagnosing schizophrenia in a broad environment rather than focusing on specific subtypes of schizophrenic diseases. It can affect disease progression, especially in the cognitive domain of research participants. This study excluded participants' genetic assessments, which may have affected the cognitive performance of each individual prior to exercise engagement. The assessment of heart rate during physical exercise training remains manual. In the future, a more sophisticated technology for monitoring the heart rate is essential to provide more accurate findings. The prolonged period of the research caused some individuals to occasionally experience a sensation of boredom over their participation in the additional exercise treatment., Therefore A various activities are necessary to reduce patient saturation.

# **CONCLUSION**

The results indicated a notable enhancement in cognitive function in both the treated group, which received additional exercise training alongside risperidone therapy, and the control group, which received risperidone therapy only. A notable decrease in body weight was observed. These findings suggest that these results may offer an alternative approach for the nonpharmacological treatment of individuals with schizophrenia. This study did not consider whether each respondent was accustomed to engaging in physical activities or exercising before participating in the study. This factor may have influenced participants' physical capabilities during the intervention. Therefore, it is important for future research to consider this aspect, as previous experience with physical activity could potentially impact the effectiveness of the intervention and the participants' physical performance. It would also be wise to include genetic analysis, thereby removing any confounding variables and enabling stronger research results. The findings of this study are expected to improve theoretical frameworks related to exercise training, specifically regarding the implementation process and the processes by which exercise may boost cognitive function and neuroplasticity. These data may function as extensive instructional tools for both families and patients. Incorporating physical activity into lifestyle choices is feasible. In the realm of outpatient care, consistent participation in physical exercise activities is recommended.

# REFERENCES

- Alan, B. and Kültür, S. (2013). Change in metabolic parameters and weight in response to risperidone monotherapy in young children with nonpsychotic disorders: a prospective open-label study. Child and Adolescent Mental Health, 20(1), 20-25. https://doi.org/10.1111/camh.12033
- Ali, I. (2014). Impact of combination interferon therapy on the body weight, body fat and lean body mass of chronic hcv infected patients. Journal of Antivirals & Antiretrovirals, 06(01). https://doi.org/10.4172/jaa.1000087
- Andrews, S. C., Curtin, D., Hawi, Z., Wongtrakun, J., Stout, J. C., & Coxon, J. P. (2020). *Intensity Matters: High-Intensity Interval Exercise Enhances Motor Cortex Plasticity More Than Moderate Exercise*, 30(1), 101-112. Cerebral Cortex.
- Bardazzi, F., Balestri, R., Baldi, E., Antonucci, A., Tommaso, S., & Patrizi, A. (2010). Correlation between bmi and pasi in patients affected by moderate to severe psoriasis undergoing biological therapy. Dermatologic Therapy, 23, S14-S19. https://doi.org/10.1111/j.1529-8019.2009.01281.x
- Chen, K., Zhang, X., Feng, W., Li, Y., Xiu, M., & Chen, D. (2019). Effects of risperidone on glucose lipid metabolism and bodyweight in drug-naïve first episode chinese han patients with schizophrenia: a prospective study. https://doi.org/10.21203/rs.2.12083/v1
- Cooper, S., Reynolds, G., Barnes, T., England, E., Haddad, P., Heald, A., ... & Smith, J. (2016). Bap guidelines on the management of weight gain, metabolic disturbances and cardiovascular risk associated with psychosis and antipsychotic drug treatment. Journal of Psychopharmacology, 30(8), 717-748. https://doi.org/10.1177/0269881116645254
- Dowthwaite, J., Rosenbaum, P., Sames, C., & Scerpella, T. (2014). *Muscle function, dynamic loading, and femoral neck structure in pediatric females*. Medicine & Science in Sports & Exercise, 46(5), 911-919. https://doi.org/10.1249/mss.0000000000000191
- Girdler, S. J., Confino, J. E., & Woesner, M. E. (2019). Exercise As a Treatment for Schizophrenia: A

- *Review*, 49(1), 56–69. Psychopharmacology Bulletin.
- Griwijoyo, S., & Sidik, D. J. (2013). *Ilmu Faal Olahraga (Fisiologi Olahraga): Fungsi Tubuh Manusia pada Olahraga untuk Kesehatan dan Prestasi*. Bandung: Remaja Rosdakarya
- Højman, P., Fjelbye, J., Zerahn, B., Christensen, J., Dethlefsen, C., Lonkvist, C., ... & Gehl, J. (2014). Voluntary exercise prevents cisplatin-induced muscle wasting during chemotherapy in mice. Plos One, 9(9), e109030. https://doi.org/10.1371/journal.pone.0109030
- Keefe, R. S. E., Poe, M., Walker, T. M., Kang, J. W., & Harvey, P. D. (2006). The Schizophrenia Cognition Rating Scale: An Interview-Based Assessment and Its Relationship to Cognition, Real-World Functioning, and Functional Capacity, 163(3), 426–432. American Journal of Psychiatry.
- Kemenkes RI. (2018). *Laporan Nasiona Riset Kesehatan Daerah 2018*. Badan Penelitian dan Pengembangan Kesehatan.
- Kusumawardhani A.A.A.A, Dharmono S, D. H. (2011). Konsensus Penatalaksanaan Gangguan Skizofrenia (Pertama). Perhimpunan Dokter Spesialis Kedokteran Jiwa Indonesia Jakarta (PDSKJI).
- Kong, J., Jok, L., Ayub, A., & Bau, R. (2017). Worksite weight management program. Nutrition & Food Science, 47(4), 490-510. https://doi.org/10.1108/nfs-08-2016-0132
- Libowitz, M. and Nurmi, E. (2021). The burden of antipsychotic-induced weight gain and metabolic syndrome in children. Frontiers in Psychiatry, 12. https://doi.org/10.3389/fpsyt.2021.623681
- Li, L., Li, X., Wyler, S., Chen, X., Wan, R., Arnold, A., & Liu, C. (2021). The atypical antipsychotic risperidone targets hypothalamic melanocortin 4 receptors to cause weight gain. The Journal of Experimental Medicine, 218(7). https://doi.org/10.1084/jem.20202484.
- Liu, H., Yu, R., Gao, Y., Li, X., Guan, X., Thomas, K., & Zhang, X. (2022). Antioxidant enzymes and weight gain in drug-naive first-episode schizophrenia patients treated with risperidone for 12 weeks: a prospective longitudinal study. Current Neuropharmacology, 20(9), 1774-1782. https://doi.org/10.2174/157015 9x19666210920090547
- National Alliance on Mental Illness. (2022). What is Schizophrenia? NAMI: National

- Alliance on Mental Illness. Diakses dari https://www.nami.org/About-Mental-Illness/Mental-HealthConditions/Schizophrenia.
- National Institute of Mental Health. (2022). *Schizophrenia*. Diakses dari https://www.nimh.nih.gov/health/topics/schizophrenia.
- Oka, T., Nishimura, Y., Zang, L., Hirano, M., Shimada, Y., Wang, Z., ... & Tanaka, T. (2010). Diet-induced obesity in zebrafish shares common pathophysiological pathways with mammalian obesity. BMC Physiology, 10(1). https://doi.org/10.1186/1472-6793-10-21
- Owen, M J et al. (2004). The Molecular Genetics of Schizophrenia: New Findings Promise New Insights, 9(1): 14-27. Molecular Psychiatry. doi:10.1038/sj.mp.4001444
- Qiu, Y., Dong, Y., Sun, W., Li, G., Li, M., Zhao, Y., & Li, J. (2023). Metabolic biomarkers of risperidone-induced weight gain in drugnaïve patients with schizophrenia. Frontiers in Psychiatry, 14. https://doi.org/10.3389/fpsyt.2023.1144873
- Rahardjo, S., Herdaetha, A., & Sudiyanto, A. (2008). *Uji Validitas Schizophrenia Cognitive Rating Scale Versi Indonesia*.
- Soe, A. (2024). Metabolic effects of risperidone on patients with psychosis in a tertiary care

- hospital of myanmar. GSC Biological and Pharmaceutical Sciences, 26(3), 183-189. https://doi.org/10.30574/gscbps.2024.26.3.0105
- Stahl, S. M. (2013). Stahl's Essential Psychopharmacology Neuroscientific Basis and Practical Applications (4th ed.). Cambridge University Press.
- Stępnicki, P., Kondej, M., & Kaczor, A. A. (2018). *Current Concepts and Treatments of Schizophrenia*, 23(8). Molecules. https://doi.org/10.3390/molecules23082087.
- Viljoen, M., & Roos, J. L. (2020). *Physical Exercise* and The Patient with Schizophrenia, 49(12): 803-808. Australian Journal of General Practice. doi:10.31128/AJGP-04-20-5384
- Wan, X., Zhou, F., Huang, X., Yang, H., Wang, L., Shi, Y., & Lin, S. (2019). Risperidone stimulates food intake and induces body weight gain via the hypothalamic arcuate nucleus 5-ht2c receptor—npy pathway. CNS Neuroscience & Therapeutics, 26(5), 558-566. https://doi.org/10.1111/cns.13281
- Weaver, Samuel R. et al. (2021) Cerebral Hemodynamic and Neurotrophic Factor Responses Are Dependent on the Type of Exercise. Vol. 11. Frontiers in Physiology. doi:10.3389/fphys.2020.609935