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Combination of intensity and weekly duration of aerobic exercise to efficiently improve negative symptoms in individuals with schizophrenia

Bachelor's thesis in Human Movement Science
Supervisor: Mireille Christine Petrine von Beekvelt
Co-supervisor: Karin Roeleveld
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Bachelor's thesis

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Abstract

Schizophrenia is a complex brain disorder affecting about 0.32% of the population. While a cure remains elusive, research focuses on enhancing treatment methods. Schizophrenia has a significant impact on life expectancy due to unhealthy habits and diverse symptoms. Negative symptoms, like apathy, contribute to a sedentary lifestyle. Aerobic exercise shows promising results in improving negative symptoms in schizophrenia. However, the optimal intensity and duration of exercise for alleviating negative symptoms in individuals with schizophrenia remain unknown. This resulting in the research question being: *what is the most optimal combination of intensity and weekly duration of aerobic exercise to efficiently improve negative symptoms in individuals with schizophrenia?* Eight studies involving 433 patients demonstrated that aerobic exercise can reduce negative symptoms. Incorporating aerobic exercise in schizophrenia treatment has the potential to enhance symptoms and overall well-being, however the results did not find a specific combination between intensity and duration that is more optimal for the reduction of negative symptoms. Due to limitations and lack of information provided by the studies, further research is needed to establish specific guidelines and better answering the research question.

Abstrakt

Schizofreni er en kompleks psykisk lidelse som påvirker omtrent 0,32% av befolkningen. Mens en kur fortsatt er vanskelig å oppnå, fokuserer forskningen på å forbedre behandlingsmetoder. Schizofreni har en betydelig innvirkning på forventet levealder på grunn av usunne vaner og ulike symptomer. Negative symptomer, som apati, bidrar til en inaktiv livsstil. Tidligere forskning indikerer at aerob trening kan ha lovende resultater i behandlingen av negative symptomer for schizofreni. Imidlertid er den mest optimale intensiteten og varigheten av trening for å lindre negative symptomer hos personer med schizofreni fortsatt ukjent. Dette resulterer i forskningsspørsmålet: *hva er den mest optimale kombinasjonen av intensitet og ukentlig varighet av aerob trening for å effektivt forbedre negative symptomer hos personer med schizofreni?* Åtte studier med totalt 433 deltakere viste at aerob trening kan redusere negative symptomer. Å inkludere aerob trening i behandlingen av schizofreni har potensiale til å forbedre symptomer og generell trivsel. Imidlertid fant ikke resultatene en spesifikk kombinasjon av intensitet og varighet som er mer optimal for å redusere negative symptomer. På grunn av begrensninger og manglende informasjon fra studiene, kreves det

ytterligere forskning for å etablere spesifikke retningslinjer og bedre besvare forskningsspørsmålet.

Key words: Aerobic exercise, duration, intensity, PANSS & schizophrenia.

1. Introduction

Schizophrenia is a psychosis disorder that affects approximately 0.32% of the world´s population, making it one of the less common mental disorders (1). Despite its lower prevalence, schizophrenia is often considered one of the more severe mental disorders. Schizophrenia is a chronic brain disorder and consist of a diversity in symptoms and affect people differently (2, p. 561-562). Presently, there is no known cure for schizophrenia. Research done today is therefore focused on safer and better treatment (3), which leads to a better way of coping with the disorder rather than to cure it. This approach is mainly due to the complexity of the disorder and the unknown casual mechanisms behind it (4).

The severity of schizophrenia is further highlighted by its impact on life expectancy. Research has revealed that individuals with schizophrenia have a life expectancy that is 10-25 years shorter than the general population (5). Unhealthy lifestyle habits are one of the most reasonable explanations for these negative numbers. Previous studies indicated that people with schizophrenia are more prone to engaging in detrimental habits, such as smoking and excessive alcohol consumption, as well as experiencing negative side effects from antipsychotic medications. Research has also shown that physical inactivity is a major prominent factor in lifestyle habits for this group (6).

For a better understanding and simplification of this complex disorder, it is common in research settings to divide the symptom picture into three categories. One widely used assessment tool is the Positive and Negative Syndrome Scale (PANSS), considered as a gold standard for assessing treatment efficacy (7). The first category is positive symptoms, which consist of symptoms that add a feeling or sensitivity to the experience that isn’t really there, such as hallucinations and delusions (8). These symptoms are mostly treated with medications (9). The second category is negative symptoms, which have proven to be more difficult to treat with medications. These symptoms subtract feelings and sensitivity from the experience of the surrounding environment. PANSS addresses seven different negative symptoms:

blunted affect, emotional withdrawal, poor rapport, passive-apathetic social withdrawal, difficulty in abstract thinking, lack of spontaneity and flow of conversation, and stereotyped thinking (8). The third category of symptoms in schizophrenia pertains to general psychopathology and refers to symptoms that are commonly observed in various mental disorders. These symptoms often arise as a result of other mental disorders (10). Alongside the general psychopathology, the positive symptoms will not be further emphasized.

PANSS evaluates 30 psychiatric parameters: 7 for positive symptoms, 7 for negative symptoms, and 16 for general psychopathology. Each item is rated on a scale of 1 to 7, indicating increasing levels of psychopathology. The ratings are as follows: 1 = absent, 2 = minimal, 3 = mild, 4 = moderate, 5 = moderate-severe, 6 = severe, and 7 = extreme. It's important to note that scores for positive symptoms, negative symptoms, and general psychopathology are independent, meaning a high score in one does not necessarily indicate a high score in the others (11).

The precise mechanisms or aspects of schizophrenia that lead to the unhealthy lifestyle observed in individuals with the disorder are not fully understood. However, it is hypothesized that negative symptoms play a significant role. When addressing the substantial inactivity within this group, it is reasonable to assume that negative symptoms such as emotional withdrawal, poor rapport, and passive-apathetic social withdrawal contribute to maintaining a sedentary lifestyle. Decreasing these negative symptoms may potentially be beneficial in increasing lifespan and improving overall quality of life, but how can this be achieved?

Aerobic exercise is known to have positive effects on schizophrenia and other mental disorders due to various physiological adaptations resulting from the exercise. One of these responses is the release of endorphins, which serve multiple functions such as pain reduction, euphoric feelings, stress and anxiety reduction, depression alleviation, improved self-esteem, and better sleep (12). Additionally, aerobic exercise provides several other health benefits, including increased energy, strengthened heart, muscles, and skeleton, lowered blood pressure, and reduced body fat. Regular cardiovascular exercise also helps reduce the risk of cardiovascular diseases, which schizophrenic patients are more susceptible to compared to the general population (12,13).

Previous studies have indicated that physical activity, specifically aerobic exercise, may improve negative symptoms in individuals with schizophrenia (14). By introducing aerobic exercise, it can initiate a positive spiral that benefits both negative symptoms and overall lifestyle. However, implementing a beneficial exercise program for this group has proven to be a challenge due to the complexity of the disorder and practical considerations (15). One possible reason for this challenge is the lack of knowledge on how to develop an exercise program that specifically suits people with schizophrenia. An important factor to consider when developing such a program, is the total workload. The total workload encompasses exercise intensity, frequency, and duration, and plays a crucial role for several reasons. For example, it helps determine an exercise program that provides a suitable level of overload, which is essential for health improvements. Having knowledge about the appropriate workload that is suitable for people with schizophrenia would make it easier to adjust and strive for a more optimal exercise program. Therefore, the research question that arises is: *What is the most optimal combination of intensity and weekly duration of aerobic exercise to efficiently improve negative symptoms in individuals with schizophrenia?* This question aims to explore and hopefully identify the optimal combination of frequency, and duration of aerobic exercise that can effectively improve the negative symptoms.

2. Method

The literature search was conducted on several databases, including Embase, PubMed, Web of Science, and SPORTDiscus. All databases were searched using the same keywords and search terms, starting with "schizophrenia" in the title. Then combined this with various endurance-based activities using "OR" to capture as many relevant studies as possible, including "cardio training," "endurance training," "jogging," "running," "brisk walk" and "interval training" in the abstract. To ensure consistency in the results, it was also added "positive and negative syndrome scale," "PANSS," "negative symptoms," or "positive symptoms" in the abstract. The search resulted in 87 articles across the four databases, which eight was included. Out of the 79 excluded studies, 24 were excluded due to inadequate results, (didn't use PANSS or SANS) 27 studies involved interventions other than endurance training. Three studies included patients with mental disorders other than schizophrenia. Seven studies were incomplete, and 18 studies had other interventions than training, such as new medication or cognitive therapy.

The inclusion criteria for this study required that participants had a diagnosis of schizophrenia and engaged in some form of endurance-based activity during the intervention period. The results of the study had to include individual scores for negative symptoms using PANSS or the Scale for Assessment of Negative Symptoms (SANS), with both baseline and post-intervention scores reported. On the other hand, studies were excluded if they included patients with other mental disorders or did not engage in endurance-based activities or had interventions other than endurance-based activity. Also excluded studies that did not report or present SANS or PANSS scores.

The Summated-Heart-Rate-Zones (SHRZ) model (16) for intensity was utilized to determine the exercise intensity levels in each of the studies conducted.

The studies that used SANS were converted into PANSS by using a converter for a more accurate comparison. This was made by *van Erp et al.* (17) to make it easier to compare results between the two symptom-scales. The converter used in this instance can be found on SANS to PANSS converter.

2.1 Meta analysis

The results of the studies were gathered in an Excel spreadsheet. There was then conducted a meta analysis with IBM SPSS Statistics Data Editor, version 29.0 to find out the overall results of the studies, seeing how physical exercise can reduce the negative symptoms in schizophrenic patients. The results were then presented in a forest plot to visualize the results from each study. The boxes in the forest plot have different colours to determine what work duration the subjects of the studies trained in.

3. Results

Eight studies were included, (18–25) and combined they presented results from 433 patients. These are split into an intervention group consisting of 216 patients, and a control group consisting of 217 patients. Four studies did not specify what intensity the exercise program utilized, one of which was assumed to be in a low intensity, and another was assumed to be in a high intensity zone based on the description of the training program, three studies were in the low-moderate intensity zone, one study was in the moderate intensity zone (see *table 1*). The duration of each training session varied from 20 – 60 minutes, with a frequency of two to four times a week, for eight to 24 weeks. Total weekly work duration varied form 90 minutes up to 180 minutes. However most studies either had 90 minutes (four studies) or 120 minutes (three studies). Only one study had a training program with a total weekly work duration of 180 minutes. The different total weekly duration is categorized by different colours in *Table 1*, *2* and *Figure 1*.

3.1 Table 1: Study design, exercise methods and training intensity

Table 1: overview of the primary studies used in this article; each row indicates a different study. Each column indicates different important factors in each study (study design, study size, exercise method and work duration, control group activity and training intensity of the subject group). The study with the blue background has a work duration of 180 min per week. The studies with the green background has a work duration of 120 min per week. The studies with the red background has a work duration of 90 min per week. Heart Rate Max has been shortened to HRM. The table continues the next three pages.

Study	Study Design	Population and Study Size	Age	Exercise Method and Work Duration	Control Group Activity	Training Intensity of the Subject Group
Curcic et al 2017	RCT	N=80-40/40	25-65	Jogging or walking on a treadmill 45 min 4 times/wk for 12 weeks Total duration: 180 min per week Does not describe minimum requirements of participation	Treatment as usual	Low to Moderate 65-75% of HRM
Shimada et al 2019	Pilot-RCT	N=31-16/15	20-65	Jogging or walking on a treadmill or cycling on an ergometer cycle 60 min 2 times/wk for 12 weeks Total duration: 120 min per week Must participate in 75% of the training program	Treatment as usual	Low to Moderate 60-80% of aerobic capacity.
Scheewe et al 2013	RCT	N=63-31/32	20-40	Cardiovascular exercise, including six muscle strength exercises (3 sets x 10-15 reps) for variation 60 min 2 times/wk for 24 weeks Total duration: 120 min per week Must particate in 50% of the training program	Occupational therapy, painting, reading and computer activities. (Allowed a maximum of 60 minutes weekly activity)	Very Low – Low – Moderate Week 1-3 45% of HRM Week 4-12 65% of HRM Week 12-26 75% of HRM

Acil et al 2008	RCT	N=30-15/15	21-45	Aerobic exercise – work method not specified 40 min 3 times/wk for 10 weeks Total duration: 120 min per week Does not describe minimum requirements of participation	Treatment as usual	Not specified Heart rate not exceeding 220-age
Malchow et al 2015	RCT	N=43-22/21	18-60	Ergometer cycle 30 min 3 times/wk for 12 weeks Total duration: 90 min per week Does not describe minimum requirements of participation	Table soccer/foosball	Moderate Individually defined intensity based on blood lactate (2 mmol/l) and *Borg scale*
Khonsari et al 2021	Case Control RCT	N=40-20/20	18-40	A combination of ergometer cycle, invisible jump rope and jogging in place, cycle at approximately 75 rpm for 12 min, speed reduction every 3 minutes Invisible jump rope for 10 min approximately 150 jumps – 5 sets 1 min jog in place between every set Finish with 8 minutes of jogging in place 30 min 3 times/wk for 8 weeks Total duration: 90 min per week Does not describe minimum requirements of participation	Treatment as usual	Not specified Assumed moderate to high intensity

Loh et al 2015	Pilot-RCT	N=100-48/52	23-65	Walking 3 times/wk, gradual increase in duration of walks First four weeks: 20 min walk Total duration: 60 min per week Five to eight weeks: 30 min walk Total duration: 90 min per week Nine to twelve weeks: 40 min walk Total duration: 120 min per week Average total duration: 90 min per week Does not describe minimum requirements of participation	Treatment as usual	Not specified Assumed low intensity
Wang et al 2018	Single Blinded RCT	N=46-24/22	38 (mean age)	30 min aerobic exercise 3 times/wk for 12 weeks Exercise method not specified Total duration: 90 min per week Must participate in at least 60% of the training program	Stretching and toning; 30 min recorded program, 14 stretching and toning exercises. Total work duration/wk: 90 min (but not endurance)	Not specified Individual intensity based on 220-age

Table 1 shows how the studies were conducted, the number of participants, their age and the activity the intervention and control groups underwent through the study period including the intensity of their activities. Four of the studies conducted the activity at a moderate intensity, one used low intensity, one used an assumed moderate-high intensity, and two studies did not specify the intensity zone the subjects were training in. For those two studies, intensity was based on the individual´s estimated maximum heart rate calculated using the formula 220 minus age. The colours in the table represents the total work duration per week. Red indicates 90 minutes, green indicates 120 minutes and blue indicates 180 minutes for total work duration per week. *Loh* (2015) had an increased work duration as the study progressed, but the average work duration throughout the study period was 90 min/wk, for this reason it is being placed in the red category. Only three of studies describes the minimal required amount of participation. *Shimada* (2019) required at least 75% participation, *Scheewe* (2013) required 50% participation and *Wang* (2018) required 60% participation.

3.2 Table 2: Results from the studies

*Table 2: overview of the recorded mean PANSS negative score (PNS) from the included studies. The table shows the results from both the subject groups (SG) and the control groups (CG) at baseline and after the follow-up. The table also includes the standard deviation in the parenthesis. The column with the mean negative score after the follow-up also includes the difference between the changes (DBC) in PNS at baseline and the after the follow-up between SG and CG. The P-value in the far-right column represents if there is a significant difference between the two means after follow-up. *=P-value<0.05, **=P-value<0.001. ΔSG is change in PNS from baseline to follow-up. ΔCG is change in PNS from baseline to follow-up.*

Study	Subject Mean PNS Baseline (SD)	Subject Mean PNS After Follow-Up (SD)	Control Baseline Mean PNS (SD)	Control Mean PNS After Follow-Up (SD)	P- value: SG - CG DBC=ΔSG —ΔCG
Curcic et al 2017	22.6 (7.1)	16.8 (5.5) *ΔSG: -5.8***	21.2 (9.1)	18 (6.6) *ΔCG: -3.2*	*P= 0.41* DBC: -2.6
Shimada et al 2019	27.4 (5.7)	21.4 (5.3) *ΔSG: -6.0**	26 (3.1)	25 (4.4) *ΔCG: -1*	*P<0.05* DBC: -5.0
Scheewe et al 2013	19.3 (6.1)	17.8 (4.9) *ΔSG: -1.5*	16.1 (5.2)	17.2 (5.8) *ΔCG: +1.1*	*P=0.65* DBC: -2,6
Acil et al 2008	15.2 (12.8)	12.2 (11.2) *ΔSG: -3.0*	17.9 (12.8)	18.9 (13.2) *ΔCG: +1*	P=0.14 DBC: -4.0
Malchow et al 2015	20.1 (9.1)	17.2 (7.7) *ΔSG: -2.9*	18.7 (8.9)	18.8 (7.5) *ΔCG: +0.1*	P=0.5 DBC: -3.4
Khonsari et al 2021	23.8 (5.9)	11.3 (2.9) *ΔSG: -12.5***	24.7 (5.4)	19.4 (6.5) *ΔCG: -5.3**	P<0.001 DBC: -7,2
Loh et al 2015	9 (3.8)	8 (2) *ΔSG: -1*	11 (8)	10.5 (6) *ΔCG: -0.5*	P<0.05 DBC: -0,5
Wang et al 2018	21.9 (8.7)	17.3 (7.2)	21.1 (7.9)	21.9 (8.2)	P<0.05

		*ΔSG: -4.6**		*ΔCG: +0.8*	DBC: -5,5

Table 2 displays the mean PNS of each of study from baseline to follow-up for both the intervention and control groups. Each study shows a decrease in PNS for the intervention group after the follow-up period, while the control groups had varying results. Some of the control groups have a slight increase in the PNS, while some show a slight decrease. The colour scheme in *Table 2* is the same as in *Table 1,* distinguishing between total work duration per week. The results indicates that physical activity at any intensity and all the different work durations decreases the PNS for the schizophrenic patients. *Khonsari* (2021) had the most reduction in the PNS out of all the studies, and *Loh* (2015) had the least reduction. The average mean reduction in the PNS from each study combined was at 5,7. The blue category had an average reduction of 5,9 points, the green category had an average reduction of 3,5 points and the red category had an average reduction of 5,3 points in PNS. Every study showed a DBC reduction, which means that all the SG had a bigger reduction in PNS on average within each study.

Curcic (2017) had a statistically significant change in PNS between baseline and follow-up with a mean reduction of 5.9 for the subject group. It also had a reduction of 3.3 PNS in the control group. That study had a DBC reduction of 2.6 PNS, which made the difference between the SG and CG not statistically significant. *Shimada* (2019) had a reduction in SG at 6 PNS which was a statistically significant change. There was also a significant difference between SG and CG in PNS. *Scheewe* (2013) had a reduction in SG at 1.5 PNS. The difference between SG and CG was not significant. DBC in *Scheewe* (2013) was at -2.6 PNS. *Acil* (2008) had no significant changes. Here the p-value between SG and CG was at 0.14 with a DBC at -4 PNS. *Malchow* (2015) had no significant changes. Here the p-value between SG and CG was at 0.5 with a DBC at -3.4 PNS. *Khonsari* (2021) had a significant reduction between baseline and follow-up for the SG at 12.5 PNS for the SG. The CG also had a significant reduction at 5.3 PNS between baseline and follow-up. The BDC in this study was at -7.2 PNS, this was statistically significant with a p-value<0.001. *Loh* (2015) had no significant changes between baseline and follow-up for any of the groups. The p-value between SG and CG was below 0.05, with a DBC at -0.5. *Wang* (2018) had a significant reduction between baseline and follow up for the SG at 4.6 PNS with p-value<0.05. There was also a p-value<0.05 between SG and CG with a DBC of -5.5.

3.3 Figure 1: Forest Plot

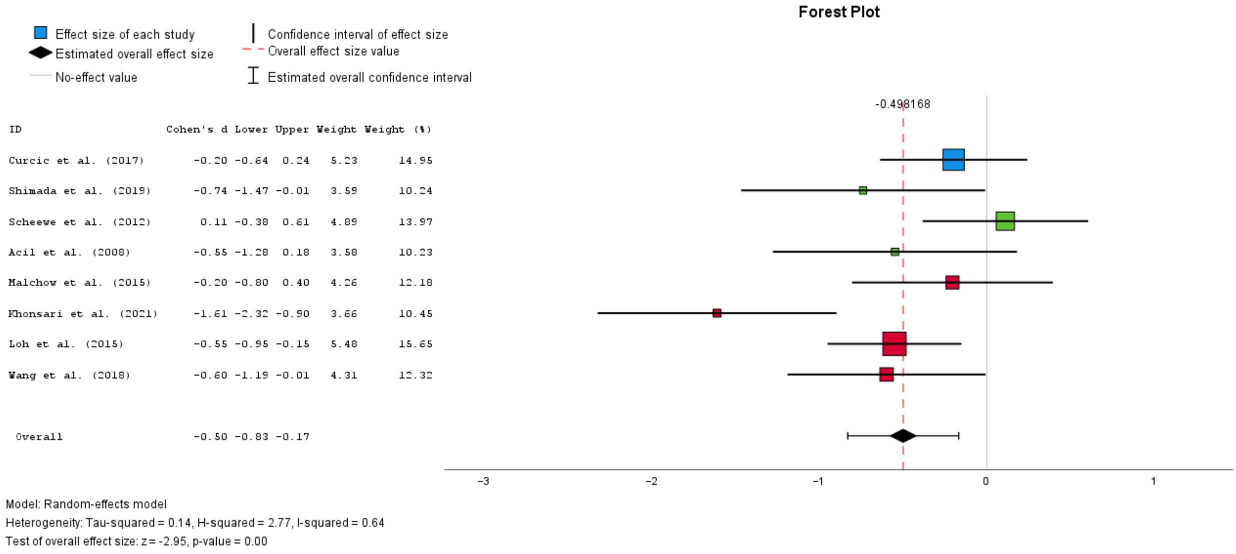

Figure 1: Forest plot of the meta analysis addressing how PA reduces PNS in schizophrenic patients based on the PNS after the follow-up in the subject group and the control group. The sizes of the boxes indicates the study size and weight of each study, the black line represents the 95% confidence interval, if the confidence interval line crosses the line of null effect, the results from the study is not statistically significant. The overall effect size is shown by the black diamond at the bottom. If the study is on the left side of the null effect line, the results from the study favours the subject group, and if the study is on the right side of the null effect line it favours the control group. On the left side of the figure the name of the individual studies are shown. The colours of the boxes represents which work duration category the subject group exercised in during the intervention. The colours are the same as in Table 1 and 2.

The forest plot shows the effect of each study and how they compare to each other, and whether it favours the SG or the CG. The overall study effect shows how PA decreases the mean PNS compared to the CG, showed by the black diamond in the plot. The plot uses a random-effects model assuming that the included studies are not estimating the same effect, since the study designs are different. The plot shows the individual studies, their size and the confidence interval. The colour scheme is the same as in *Table 1* and *2* differentiating between total work duration per week. Every study except *Scheewe* (2013) shows a lower PNS value compared to the control group. The black lines that crosses the boxes which shows the study size is the confidence interval of 95%. If the confidence interval line crosses the line of null effect, that means that the result of the study is not statistically significant. The studies where this happens are *Curcic* (2017), *Scheewe* (2012), *Acil* (2008) and *Malchow* (2015). The other studies shows results that are statistically significant (p-value < 0.05). The overall effect is also statistically significant. The heterogeneity of the studies are at 64%, shown by the I-squared value, which could show a substantial heterogeneity. This means that there is a difference between the included studies.

4. Discussion

4.1 Total duration effect on PANSS negative, what the results are saying

The forest plot in the meta analysis examines if PA has an overall effect on PNS. Every study showed a decreased DBC in *Table 2*, but in the instance of Scheewe (2013), the box on the forest plot ended up on the right side of the null effect line. This is because the CG had a general lower PNS compared to the SG, but it did not have a larger decrease. In fact the control group had an increase in PNS after the follow-up showed in *Table 2*.

The results from *Table 2* and *Figure 1* further supports previous research findings that aerobic exercise appears to be beneficial in treating negative symptoms in individuals with schizophrenia. When viewing the total weekly work duration, one can see that all the studies with a 90 minute weekly duration, tend to have a positive effect on negative symptoms. Here 3 out of 4 studies showed a significant difference in PNS between SG and CG. *Khonsari* (2021) presents the biggest improvement on PNS out of all the eight studies. The rest of the studies with a duration of 90 minutes of weekly exercise duration, falls more stable around the mean difference for all studies combined.

Studies with a total weekly duration of 120 minutes demonstrate greater variation in outcomes. Among these studies, two of them show a better PNS in SG compared to CG, with one of the differences being significant. When comparing just these two studies, their mean difference is roughly equal to the studies with a 90-minute duration (*Shimada*, 2019; *Acil*, 2008). However, *Scheewe* (2013) showed a higher PNS in SG compared to CG. Reason being a general higher PNS in SG at baseline. The DBC-scores indicates that there are no differences between PNS outcomes in 90 and 120-minutes programs. This implies that developing a program within the range of 90 to 120 minutes per week can be equally efficient in reducing PNS. *Curcic* (2017) presents a lower improvement in DBC. The improvement is also not significant in itself, despite it being one of the bigger studies. This indicates that an exercise program lasting around 180-minutes per week might not be as beneficial. However, this was the only study including a 180-minutes work duration, therefore there are no other studies to support these results.

4.2 Adjusting to intensity.

The findings indicate that moderate intensity aerobic exercise has a documented effect on negative symptoms, although it remains uncertain whether higher intensity aerobic training has a similar impact. Notably, *Kohnsari* (2021) that implemented an assumed moderate-high intensity, demonstrated the largest reduction in negative symptoms based on the PNS. This could mean that facilitating for higher intensity training, could be beneficial for people with schizophrenia, rather than just increasing training hours.

The study with the second highest decrease in DBC was *Shimada* (2019), which implemented a low to moderate intensity, with a weekly duration of 120 minutes. This is contradictory to *Khonsari* (2021). The other studies that had a large decrease in DBC did not specify which training intensity the subject groups were in. This contradictory outcome makes it difficult to determine which interaction between training intensity and weekly duration has the best effect on PNS.

4.3 Sources of error

A potential source of error that may arise when studying patients with schizophrenia is the selection bias when choosing participants. If the included patients are in a better mental state compared to those who are unable to participate, it can introduce a selection bias and potentially influence the overall results of the study. The challenge lies in finding ways to include individuals who are unable to engage in the physical activities required by other participants. For practical reasons this is something that can be hard to achieve due to the severity of the disorder, and the lack of cognitive function. Had these patients not been selected out, the number of dropouts or quality of training could be diminished.

Additionally, exclusion criteria related to lifestyle factors, such as smoking or drinking, can also affect the results (22). However, when these individuals are excluded, we only observe the impact on "healthy" individuals with schizophrenia. The outcomes for those who are most severely affected by the disorder and struggling the most may differ significantly. The results from this study selection, may therefore not be generalised for all schizophrenic patients. There were also some dropouts during the study period, this may also inflict the results in a similar way. Main reasons for dropouts were a vast downfall in mental and physical state, alongside lack of motivation and capability to complete the given program.

Another factor that can potentially lead to inaccurate results is a low criteria for participation. The studies included had a mild mandatory participation demand. This could alter the amount of exercise the patients participated in and could also alter the results. For example, *Scheewe* (2013) only had a 50% participation limit meaning the patients in the intervention group only needed to participate on half the exercises to be included in the results. Considering that this article is looking at exercise duration, a low limitation of participation gives room for possible misinformation. Others did not present a lower limit of participation (18–22), therefore it's hard to say the minimal amount of exercise the patients participated in.

Implementing a training program, one must also consider the potential influence of confounding factors that could reduce the PNS. In studies related to schizophrenia, an example of a confounding factors could be a shift in the environment, such as exercising outdoors, in a group setting, or under the guidance of a trainer. Such environmental changes may introduce a new social setting that could positively impact the mental state of the patients. Additionally, individuals undergoing the program might unknowingly adopt other lifestyle changes that could be equally or even more advantageous in enhancing PNS, beyond the effects of aerobic exercise alone.

Another confounding factor could be CG exposure. This could potentially lead to incorrect differences between the groups. This allows for a comparison between different types of exposure. For instance, in the study conducted by *Wang* (2018), the CG underwent stretching and toning exercises in addition to treatment as usual. However, this comparison between aerobic exercise and toning/stretching does not align with the original research question, yielding results that are incongruent.

The last source of error to be discussed in this article is measurement errors. Measurement errors can occur when conducting research on schizophrenic patients, including errors in measuring PANSS, assessing the intensity level of training programs, and accurately measuring the duration of participants' engagement in the training program. Misinterpretation of results and the information presented in each study can also lead to divergent conclusions that may not reflect the actual occurrences. Moreover, the absence of well-established, standardized, and comparable cut-off values for each intensity level across all eight studies can pose challenges. For instance, when studies employ formulas like 220-age or a percentage of aerobic capacity, they often lack precise and substantial information. Consequently, researchers must rely on other components of the exercise programs to estimate intensity, which becomes problematic when the studies fail to provide detailed information about the participants' training background. This issue is exemplified by the insufficient information regarding exercise intensity in some of the included studies. Additionally, an imprecise and incomplete literature search may result in the exclusion of relevant studies pertinent to the research question.

4.4 Further research

Based on the sources of error and lack of fulfilling results from former studies, further research within the field is necessary. However, to conduct further studies that's suitable to answer the research question, it's crucial to have a more fulfilling study design that includes and compares, different intensity groups, exercise frequencies and training duration. The studies should also be of a larger sample size, as this increases the validity by minimizing the risk of being affected by extreme values.

Conclusion

Aerobic exercise has shown positive effects on schizophrenia and other mental disorders. It can help reduce negative symptoms, improve overall health, and mitigate the risk of cardiovascular diseases. However, implementing an effective exercise program for individuals with schizophrenia is challenging due to the complexity of the disorder and practical considerations. The results from *Table 2* and the meta analysis showed that regular PA has a positive effect on the PNS and could be a good implementation as a treatment for schizophrenic patients in addition to medicinal treatment. There is also not a standardized method that is used in schizophrenia research. This makes it hard to compare the results for different studies and improve them. In conclusion, aerobic exercise has the potential to improve negative symptoms in individuals with schizophrenia. However, more research is needed to determine the most efficient weekly workload or work duration that optimally benefits these patients. Developing tailored exercise programs that suit the specific needs of individuals with schizophrenia could enhance their overall well-being and quality of life.

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