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The influence of physical activity on the health and treatment of schizophrenia patients

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Abstract

Schizophrenia is a chronic and severe mental illness that affects multiple areas of life. Patients with schizophrenia are prone to developing serious and even fatal disorders when it comes to their physical health. They have a higher mortality risk and an average of 14,5 years of potential life lost compared to the general population. Physical activity decreases mortality, reduces cardiovascular risk, and improves mental health. Within this article, we explore the topic of physical activity and its influence on the physical and mental health of schizophrenia patients and their treatment.

Keywords: schizophrenia; physical activity; physical health; mental health;

Introduction

The role of physical activity in maintaining physical and emotional well-being is undeniable and prominent. An overwhelming majority of the population can profit from including more movement in their lives. [1] Physical activity reduces the risk of cardiovascular diseases, type 2 diabetes, and cancer, [2] and leads to an overall decrease in mortality. [3] Regular exercising improves mental health by reducing depressive symptoms and leading to an improvement in anxiety and panic disorder. [4] Moderate levels of exercise enhance mood and help sustain elevated levels thereof. [5] Participating in any form of sport improves mental health and social outcomes among adults. [6] With so many benefits, physical movement is also likely to improve the quality of life of people with schizophrenia and have a positive influence on their treatment. This is why we set out to explore the topic of the impact of physical activity on the physical and mental health of schizophrenia patients and their treatment by conducting a review of some of the existing literature on the topic.

Symptoms

Schizophrenia is a chronic and severe mental illness represented by disturbances in perception, thought, and behavior. [7] In its course, positive and negative symptoms can be distinguished. Positive symptoms can manifest themselves as hallucinations, voices communicating with the patient or talking about him, and delusions, often paranoid ones. Negative symptoms include social withdrawal, flattened affect, as well as loss of will, drive, or sense of pleasure. [8]

Epidemiology

Schizophrenia, being a complex disease, affects multiple areas of life. Its prevalence used to be estimated at 1% in all cultures and the illness was considered to occur equally often among men and women. [8] The current view on gender distinction differs in incidence rate. According to the new data, men are moderately more inclined to develop this disorder with an occurrence peak in their early twenties compared to women for whom the peak is flatter and extended over time. [9]

Life expectancy and years of potential life lost

Schizophrenia patients have a higher mortality risk than healthy individuals. A meta-analysis of 11 studies conducted in Africa, Asia, Australia, Europe, and North America has shown that schizophrenia is associated with an average of 14.5 years of potential life lost. Among both genders, more years of life were lost by men compared to women. The average life expectancy was 64.7: 59.9 years for men and 67.6 years for women. [10] The results of another study conducted in western China including 228,572 patients with schizophrenia were even more distressing: the estimated life expectancy was 52.8 years for men and 59 years for women. [11]

The causes for the increased mortality rate can be linked to several issues. The authors of a study concerning excess early mortality in schizophrenia point out the following:

- Late diagnosis and poor treatment of physical illnesses in schizophrenia patients.
- Negative side effects of antipsychotic drugs.
- Unhealthy lifestyle among patients with schizophrenia.
- Increased risk of suicide and accidents in patients with schizophrenia in comparison to healthy people. [12]

A schizophrenia patient in the healthcare service

It is difficult for schizophrenia patients to recognize and manage their physical problems. Their search for help can be inadequate and insufficient. Despite contacting general practice quite often, schizophrenia patients encounter delays in the diagnosis and treatment of somatic disorders. [13]. Patients lack communication skills allowing them to precisely identify and describe issues and symptoms concerning their health. [14] Therefore they are at risk of experiencing undetected and untreated somatic diseases. [13] The significance of underdiagnosed disorders in schizophrenia patients is exacerbated by various medical illnesses being more common among psychiatric patients than in the general population. [14]

Cardiovascular and metabolic risk

Schizophrenia is increasingly being acknowledged as a systemic disease. [15] Cardiovascular disease is the most common cause of death in patients with schizophrenia and it was proven to occur 85% more often in this group compared to the general population. According to a large meta-analysis, people with this severe mental illness have a higher incidence regarding coronary artery disease — 64%, cerebrovascular disease — 64%, and congestive heart failure — 110% than the general population. Schizophrenia is also associated with an increased cardiovascular risk. Many modifiable cardiovascular risk factors can be seen in schizophrenia patients — such as smoking, obesity, obstructive sleep apnea, sedentary lifestyle, or poor diet. [16]

The unhealthy lifestyle is often presented as one of the factors that put schizophrenia patients at risk of developing metabolic syndrome. Its prevalence among schizophrenia patients varies between 19.4% and 68% depending on the studied population. [17] Schizophrenia patients have a higher probability of developing abdominal obesity, hypertension, low LDL-C, and hypertriglyceridemia. [18]

People with schizophrenia are more likely to become obese and have a higher average BMI than the general population. [19]

Antipsychotic treatment is another determinant shown as significant for metabolic syndrome. Side effects of antipsychotic drugs include significant weight gain, abdominal obesity, insulin resistance, lipid and glucose metabolism changes. [18] The weight gain varies depending on the drug — clozapine and olanzapine have the highest effect, quetiapine and risperidone — intermediate, while aripiprazole, amisulpride, ziprasidone, and asenapine have a small impact on weight. [17] However, schizophrenia patients are more likely to develop metabolic syndrome regardless of antipsychotic treatment — 53.8% among patients treated with clozapine and 20.7% in the control group. [13]

An American study has shown that it is not only the patients with severe psychotic disorders that are at risk of incidence of cardiovascular and/or metabolic diseases but also their families. Participants included probands with diagnoses of schizophrenia, schizoaffective, and bipolar disorders, their first-degree relatives, and healthy controls. First-degree relatives of psychosis subjects independent of any psychiatric problems or drug effects had a 1.6 times higher risk of experiencing cardio-metabolic dysfunction (defined as coronary artery disease, diabetes, hypertension, hyperlipidemia present in medical history or treated) compared to the healthy controls. The authors suggest that psychosis and cardio-metabolic dysfunction may share familial risk factors and the possibility of pleiotropic effects of their risk genes should be studied. [20]

Physical activity in schizophrenia patients

People with severe mental illness lead a more sedentary life than healthy controls. [21] and are at risk for low cardiorespiratory fitness. [22] Moreover, they engage less in moderate and vigorous physical activity. In the global systemic review and meta-analysis concerning sedentary behavior and physical levels in people with severe mental illness, schizophrenia patients were the least active when compared to people with bipolar disorder and major depressive disorder. [21]

Physical activity's impact on schizophrenia symptoms

Exercise can remarkably improve positive symptoms, negative symptoms, and verbal short-term memory; it may also attenuate the neurological deterioration associated with psychotic disorders. [23] The European Psychiatric Association's guidance on physical activity as a treatment for severe mental illness states that physical activity ought to be used as an additional treatment for schizophrenia-spectrum disorders. [24] Exercise supplementation may be beneficial and improve symptoms, global cognition, and the quality of life of people with schizophrenia-spectrum disorders. To decrease the dropout of the interventions, supervision by qualified professionals and motivational components should be included. [24]

A randomized clinical trial conducted in the Clinic for Mental Disorders in Serbia showed a notable role of physical activity in the amelioration of schizophrenia symptoms. [25] Subjects engaged in 45 minutes of physical activity, four times per week, reaching between 65 and 75% of their maximum heart rate. After a twelve weeks long program, there was a statistically significant improvement in schizophrenia symptoms compared to the control group. Moreover, the exercising participants presented a significantly increased VO2 max compared to before the 12-week period. This improvement set their results much higher than in the non-exercising group, whose change was not statistically significant. Both the test and the control group were treated with antipsychotic drugs during the experiment. [25]

Physical activity may also be a protective factor against the emergence of psychosis, but the association is unclear and needs to be examined in the future. [26] A meta-analysis of prospective studies linked physical activity with a prospectively decreased risk of incident psychosis or schizophrenia. However when adjusting the confounding factors the association was no longer upheld. [26]

The impact of physical activity on the physical health of people with schizophrenia

Individual lifestyle counseling followed by exercise interventions alone was the most effective strategy to reduce body weight in patients with schizophrenia according to a metareview of meta-analyses of randomized controlled trials conducted in 2019. [27] What is more, the inclusion of physical activity demonstrated large effects on functional exercise capacity improvement. No significant reduction in body mass index compared to the control group was observed for exercise intervention. [27]

Another systematic review and meta-analysis found cardiorespiratory fitness being significantly improved by exercise among patients with severe mental illnesses. High-intensity aerobic exercises performed three or more times per week supervised by qualified personnel anticipated a better outcome. [22] With that being achievable, cardiorespiratory fitness improvement may contribute to a reduction in premature mortality, as it appears to be a strong independent predictor of all-cause and cardiovascular disease mortality. [28,22]

Conclusions

Schizophrenia presents itself among people all over the world and influences various aspects of life. Patients suffering from this severe mental illness have a higher mortality risk and lower average life expectancy than controls. Schizophrenia is associated with increased cardiovascular risk and a higher prevalence of cardiovascular diseases compared to the general population. Schizophrenia patients are more likely to suffer from the metabolic syndrome or its characteristics than healthy controls and yet they encounter delays in diagnosis and treatment of their somatic disorders. Due to these factors, it is even more crucial to implement prevention strategies and emphasize prophylaxis among this population.

Physical activity has been proven to have a positive influence not only on the physical but also mental health of patients with schizophrenia. Evidence shows amelioration of both negative and positive symptoms, a betterment of cognition and verbal short-term memory, and an upswing in the quality of life. Physical movement has a positive impact on the risk factors of cardiovascular and metabolic diseases — it reduces body weight and improves functional exercise capacity as well as cardiorespiratory fitness. The role of physical activity as a protective factor against the emergence of psychosis and neurological deterioration, however, remains uncertain and requires further investigation.

Schizophrenia patients lead a sedentary lifestyle and are the least active among severe mental illness patients. When motivated accordingly and supervised by a qualified professional, more patients were able to better adhere to their exercise routine. Considering this, increasing health awareness and encouraging the implementation of daily physical activity among schizophrenia patients should be the doctors' priority.

Disclosure:

Author's contribution:

Conceptualization, Katarzyna Kuśmierczyk, and Patrycja Karkos; Methodology, Marta Jurga, Michał Ciołkosz, and Karolina Mikołap; Software, Arkadiusz Staroń and Elena Sztemberg; Check, Bartłomiej Gastoł and Elena Sztemberg; Formal analysis, Marta Kras, Bartłomiej Gastoł, and Filip Grajnert; Investigation, Katarzyna Kuśmierczyk, Marta Kras and Patrycja Karkos; Resources, Karolina Mikołap, Filip Grajnert, and Michał Ciołkosz; Data curation, Michał Ciołkosz, Arkadiusz Staroń and Marta Kras; Writing - rough preparation, Katarzyna Kuśmierczyk; Writing - review and editing, Katarzyna Kuśmierczyk, Marta Jurga, Patrycja Karkos, Arkadiusz Staroń, Elena Sztemberg, Karolina Mikołap, Filip Grajnert, Michał Ciołkosz, Marta Kras and Bartłomiej Gastoł; Visualization, Elena Sztemberg and Bartłomiej Gastoł; Supervision, Marta Jurga, Patrycja Karkos and Filip Grajnert; Project administration, Karolina Mikołap, Marta Jurga, and Arkadiusz Staroń; Receiving funding, not applicable;

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References:

- [2] Dhuli, K., Naureen, Z., Medori, M. C., Fioretti, F., Caruso, P., Perrone, M. A., Nodari, S., Manganotti, P., Xhufi, S., Bushati, M., Bozo, D., Connelly, S. T., Herbst, K. L., & Bertelli, M. (2022). Physical activity for health. *Journal of Preventive Medicine and Hygiene*, 63(2 Suppl 3), E150. https://doi.org/10.15167/2421-4248/JPMH2022.63.2S3.2756
- [3] Blair, S. N., Kohl, H. W., Barlow, C. E., Gibbons, L. W., Paffenbarger, R. S., & Macera, C. A. (1995). Changes in Physical Fitness and All-Cause Mortality: A Prospective Study of Healthy and Unhealthy Men. *JAMA*, *273*(14), 1093–1098. https://doi.org/10.1001/JAMA.1995.03520380029031
- [4] Paluska, S. A., & Schwenk, T. L. (2000). Physical activity and mental health: Current concepts. *Sports Medicine*, 29(3), 167–180. https://doi.org/10.2165/00007256-200029030-00003/METRICS
- [5] Peluso, M. A. M., & Guerra de Andrade, L. H. S. (2005). PHYSICAL ACTIVITY AND MENTAL HEALTH: THE ASSOCIATION BETWEEN EXERCISE AND MOOD. *Clinics*, 60(1), 61–70. https://doi.org/10.1590/S1807-59322005000100012
- [6] Eather, N., Wade, L., Pankowiak, A., & Eime, R. (2023). The impact of sports participation on mental health and social outcomes in adults: a systematic review and the 'Mental Health through Sport' conceptual model. *Systematic Reviews*, 12(1). https://doi.org/10.1186/S13643-023-02264-8
- [7] American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders: DSM-5. American Psychiatric Association. 2013.
- [8] SCHULTZ, S. H., NORTH, S. W., & SHIELDS, C. G. (2007). Schizophrenia: A Review. *American Family Physician*, 75(12), 1821–1829. https://www.aafp.org/pubs/afp/issues/2007/0615/p1821.html
- [9] Jauhar, S., Johnstone, M., & McKenna, P. J. (2022). Schizophrenia. *The Lancet*, 399(10323), 473–486. https://doi.org/10.1016/S0140-6736(21)01730-X
- [10] Hjorthøj, C., Stürup, A. E., McGrath, J. J., & Nordentoft, M. (2017). Years of potential life lost and life expectancy in schizophrenia: a systematic review and meta-analysis. *The Lancet Psychiatry*, 4(4), 295–301. https://doi.org/10.1016/S2215-0366(17)30078-0
- [11] Liu, X., Wang, D., Fan, R., Wang, R., Xiang, H., Yang, X., & Liu, Y. (2022). Life expectancy and potential years of life lost for schizophrenia in western China. *Psychiatry Research*, 308, 114330. https://doi.org/10.1016/J.PSYCHRES.2021.114330
- [12] Laursen, T. M., Nordentoft, M., & Mortensen, P. B. (2014). Excess Early Mortality in Schizophrenia. *The Annual Review of Clinical Psychology Is Online At*, *10*, 425–473. https://doi.org/10.1146/annurev-clinpsy-032813-153657

- [13] Oud, M. J., & Meyboom-De Jong, B. (2009). Somatic diseases in patients with schizophrenia in general practice: their prevalence and health care. *BMC Family Practice*, 10, 32. https://doi.org/10.1186/1471-2296-10-32
- [14] Goldman, L. S. (1999). Medical Illness in Patients With Schizophrenia. *The Journal of Clinical Psychiatry*, 60(suppl 21), 11456. https://www.psychiatrist.com/jcp/medical-illness-patients-schizophrenia
- [15] Dieset, I., Andreassen, O. A., & Haukvik, U. K. (2016). Somatic Comorbidity in Schizophrenia: Some Possible Biological Mechanisms Across the Life Span. *Schizophrenia Bulletin*, 42(6), 1316. https://doi.org/10.1093/SCHBUL/SBW028
- [16] Goldfarb, M., de Hert, M., Detraux, J., di Palo, K., Munir, H., Music, S., Piña, I., & Ringen, P. A. (2022). Severe Mental Illness and Cardiovascular Disease: JACC State-of-the-Art Review. *Journal of the American College of Cardiology*, 80(9), 918–933. https://doi.org/10.1016/J.JACC.2022.06.017
- [17] de Hert, M., Correll, C. U., Bobes, J., Cetkovich-Bakmas, M., Cohen, D. A. N., Asai, I., Detraux, J., Gautam, S., Möller, H. J., Ndetei, D. M., Newcomer, J. W., Uwakwe, R., & Leucht, S. (2011). Physical illness in patients with severe mental disorders. I. Prevalence, impact of medications and disparities in health care. *World Psychiatry*, 10(1), 52. https://doi.org/10.1002/J.2051-5545.2011.TB00014.X
- [18] Penninx, B. W. J. H., & Lange, S. M. M. (2018). Metabolic syndrome in psychiatric patients: overview, mechanisms, and implications. *Dialogues in Clinical Neuroscience*, 20(1), 63. https://doi.org/10.31887/DCNS.2018.20.1/BPENNINX
- [19] Coodin, S. (2001). Body mass index in persons with schizophrenia. *Canadian Journal of Psychiatry. Revue Canadienne de Psychiatrie*, 46(6), 549–555. https://doi.org/10.1177/070674370104600610
- [20] Mothi, S. S., Tandon, N., Padmanabhan, J., Mathew, I. T., Clementz, B., Tamminga, C., Pearlson, G., Sweeney, J., & Keshavan, M. S. (2015). Increased cardio-metabolic dysfunction in first degree relatives of patients with psychotic disorders. *Schizophrenia Research*, *165*(1), 103. https://doi.org/10.1016/J.SCHRES.2015.03.034
- [21] Vancampfort, D., Firth, J., Schuch, F. B., Rosenbaum, S., Mugisha, J., Hallgren, M., Probst, M., Ward, P. B., Gaughran, F., de Hert, M., Carvalho, A. F., & Stubbs, B. (2017). Sedentary behavior and physical activity levels in people with schizophrenia, bipolar disorder and major depressive disorder: a global systematic review and meta-analysis. *World Psychiatry*, 16(3), 308. https://doi.org/10.1002/WPS.20458
- [22] Vancampfort, D., Rosenbaum, S., Schuch, F., Ward, P. B., Richards, J., Mugisha, J., Probst, M., & Stubbs, B. (2017). Cardiorespiratory Fitness in Severe Mental Illness: A Systematic Review and Meta-analysis. *Sports Medicine*, 47(2), 343–352. https://doi.org/10.1007/S40279-016-0574-1/FIGURES/3
- [23] Firth, J., Cotter, J., Elliott, R., French, P., & Yung, A. R. (2015). A systematic review and meta-analysis of exercise interventions in schizophrenia patients. *Psychological Medicine*, 45(7), 1343–1361. https://doi.org/10.1017/S0033291714003110

- [24] Stubbs, B., Vancampfort, D., Hallgren, M., Firth, J., Veronese, N., Solmi, M., Brand, S., Cordes, J., Malchow, B., Gerber, M., Schmitt, A., Correll, C. U., de Hert, M., Gaughran, F., Schneider, F., Kinnafick, F., Falkai, P., Möller, H. J., & Kahl, K. G. (2018). EPA guidance on physical activity as a treatment for severe mental illness: a meta-review of the evidence and Position Statement from the European Psychiatric Association (EPA), supported by the International Organization of Physical Therapists in Mental Health (IOPTMH). *European Psychiatry*, *54*, 124–144. https://doi.org/10.1016/J.EURPSY.2018.07.004
- [25] Curcic, D., Stojmenovic, T., Djukic-Dejanovic, S., Dikic, N., Vesic-Vukasinovic, M., Radivojevic, N., Andjelkovic, M., Borovcanin, M., & Djokic, G. (2017). Positive impact of prescribed physical activity on symptoms of schizophrenia: randomized clinical trial. *Psychiatria Danubina*, 29(4), 459–465. https://doi.org/10.24869/PSYD.2017.459
- [26] Brokmeier, L. L., Firth, J., Vancampfort, D., Smith, L., Deenik, J., Rosenbaum, S., Stubbs, B., & Schuch, F. B. (2020). Does physical activity reduce the risk of psychosis? A systematic review and meta-analysis of prospective studies. *Psychiatry Research*, 284, 112675. https://doi.org/10.1016/J.PSYCHRES.2019.112675
- [27] Vancampfort, D., Firth, J., Correll, C. U., Solmi, M., Siskind, D., de Hert, M., Carney, R., Koyanagi, A., Carvalho, A. F., Gaughran, F., & Stubbs, B. (2019). The impact of pharmacological and non-pharmacological interventions to improve physical health outcomes in people with schizophrenia: a meta-review of meta-analyses of randomized controlled trials. *World Psychiatry*, *18*(1), 53. https://doi.org/10.1002/WPS.20614
- [28] Lee, D. chul, Artero, E. G., Sui, X., & Blair, S. N. (2010). Mortality trends in the general population: the importance of cardiorespiratory fitness. *Journal of Psychopharmacology* (Oxford, England), 24(4 Suppl), 27–35. https://doi.org/10.1177/1359786810382057