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Mechanisms linking physical activity with psychiatric symptoms across the lifespan: a protocol for a systematic review

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ABSTRACT

Introduction Persistent psychiatric symptomatology during childhood and adolescence predicts vulnerability to experience mental illness in adulthood. Physical activity is well-known to provide mental health benefits across the lifespan. However, the underlying mechanisms linking physical activity and psychiatric symptoms remain underexplored. In this context, we aim to systematically synthesise evidence focused on the mechanisms through which physical activity might reduce psychiatric symptoms across all ages.

Methods and analysis With the aid of a biomedical information specialist, we will develop a systematic search strategy based on the predetermined research question in the following electronic databases: MEDLINE, Embase, Web of Science, Cochrane and PsycINFO. Two independent reviewers will screen and select studies, extract data and assess the risk of bias. In case of inability to reach a consensus, a third person will be consulted. We will not apply any language restriction, and we will perform a qualitative synthesis of our findings as we anticipate that studies are scarce and heterogeneous.

Ethics and dissemination Only data that have already been published will be included. Then, ethical approval is not required. Findings will be published in a peer-reviewed journal and presented at conferences. Additionally, we will communicate our findings to healthcare providers and other sections of society (eg, through regular channels, including social media).

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Strengths and limitations of this study

- This protocol has been designed according to the Preferred Reporting Items for Systematic Reviews and Meta Analyses for Protocols guidelines and guidelines of the Cochrane Effective Practice and Organisation of Care.
- This protocol presents a cautiously designed search strategy, inclusion and exclusion criteria and time-span and age-range coverage.
- A possible limitation is that included studies might be heterogeneous in the study design, data collection methods and data analysis, which might limit the ability to synthesise the results using a meta-analysis.
- The value of this systematic review depends on the quality and availability of the evidence on the topic.

INTRODUCTION

Persistent psychiatric symptomatology in childhood and adolescence predicts vulnerability to experience mental illness later in life.[1] For instance, It is known that individuals with mental illness have a decreased life expectancy of 10–15 years[2] and a lower quality of life[3] than individuals from the general population. Psychiatric symptoms are typically grouped into two broad categories (ie, internalising/emotional and externalising/behavioural).[4] Specifically, the externalising problems include a variety of disinhibited/externally focused behavioural symptoms such as conduct problems, rule-breaking behaviour, attention-deficit/hyperactivity problems. On the contrary, the internalising disorder include a variety of overinhibited/internally focused symptoms, such as depression, anxiety or somatic symptoms. Several risk factors for psychiatric symptoms have been well established in childhood (eg, poverty and social disadvantage)[5] and adulthood (eg, level of education and physical illness).[6] However, less is known about the protective factors (eg, physical activity) that might contribute to decreasing both child and adult psychopathology.

There is a growing body of literature suggesting that physical activity has a small-to-moderate positive effect on psychiatric symptoms in children and adolescents,[7–9] and in adults and older adults.[10 11] However, most of the studies have focused on exploring the effect size of the association or effect in terms

Table 1 Inclusion criteria based on PICOS strategy

PICOS	Inclusion criteria	Exclusion criteria
Population	1. All ages across the lifespan: infancy and toddlerhood (birth to age 2), preschoolers (2–5 years), children (6–11 years), adolescents (12–18 years), young and middle adults (18– 65 years), late adulthood (+65 years). 2. Human studies.	1. Studies including individuals with physical or psychological disorders diagnosed by medical records. 2. Elite athletes. 3. Animal studies.
Intervention	1. Observational studies, which explored the mechanisms through which physical activity is associated with psychiatric symptoms. 2. Studies examining the mechanisms through which physical activity has a positive effect on psychiatric symptoms.	1. Multiple health behaviour intervention studies (eg, co-interventions such as a dietary programme combined with physical activity). 2. Studies in which physical fitness (ie, capacity to perform physical activity, which refers to a full range of physiological and psychological qualities),[18] or sedentary behaviour (ie, any waking behaviour characterised by an energy expenditure ≤1.5 METs, while in a sitting, reclining or lying posture)[19] are the independent variables instead of physical activity (ie, any bodily movement produced by skeletal muscle that results in energy expenditure).[20]
Comparison	1. Not applicable.	
Outcomes	1. The subscales of internalising symptoms (ie, depression, anxiety, somatic symptoms) and externalising symptoms (ie, conduct problems, rule-breaking behaviour, attention-deficit/hyperactivity problems).	
Study design	1. Intervention studies (randomised controlled trials, non-randomised controlled trials), prospective longitudinal studies and cross-sectional studies.	1. Conference proceedings and other types of grey literature. 2. Narrative reviews, systematic reviews or meta-analyses.

MET, metabolic equivalent of task .

of dose-response, while the mechanisms underlying this relationship or effect remain underexplored. In 2016, Lubans *et al*[12] published a systematic review of the mechanisms linking physical activity and psychiatric symptoms in children and adolescents. They proposed a conceptual model, which postulated three distinct yet intertwined potential groups of mechanisms (ie, neurobiological, psychosocial and behavioural mechanisms). In brief, they identified a lack of available evidence for the specific mechanisms responsible for the effect of physical activity on mental and cognitive health in young people. Additionally, they only included intervention studies, and although this type of design can provide evidence for cause and effect, observational studies can also provide complementary information, particularly when there is a lack of evidence on the topic.

In adults, only narrative reviews,[13–15] mainly focused on cognition[13] and depression,[14 15] have explored the potential mechanisms that might link physical activity with psychiatric symptoms in adulthood. For instance, Stillman *et al*[13] suggested that physical activity might reduce depression and anxiety via psychosocial pathways (eg, mood). Additionally, Kandola *et al*[14] presented a conceptual framework of the key biological and psychosocial mechanisms underlying the relationship between physical activity and depressive symptoms in adults. However, no previous systematic reviews have been performed to synthesise the existing evidence in adults.

Understanding the mechanisms linking physical activity with psychiatric symptoms may help to explain, predict and intervene more effectively, which could stimulate the identification of cost-efficient alternative therapies for preventing and treating mental illness at all ages. To establish this evidence-based, it is imperative to synthesise and update all relevant literature mapping the mechanisms through which physical activity reduces psychiatric symptoms across the lifespan.

Objective

We aim to conduct a systematic review to explore the underlying mechanisms linking physical activity with psychiatric symptoms in humans of all ages.

Review questions

How does physical activity affect/associate with psychiatric symptoms via psychosocial, neurobiological and behavioural pathways across the lifespan?

METHODS

The present protocol follows the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) for Protocols guideline for systematic review and meta-analysis protocols.[16] We will perform the search in March 2022, and we are planning to finish the systematic review in June 2022.

Patient and public involvement

Patients and the public were not involved in the design, development, conduct, reporting or dissemination of this study.

Eligibility criteria

We will include studies based on predefined criteria as summarised in table 1 and the text.[17]

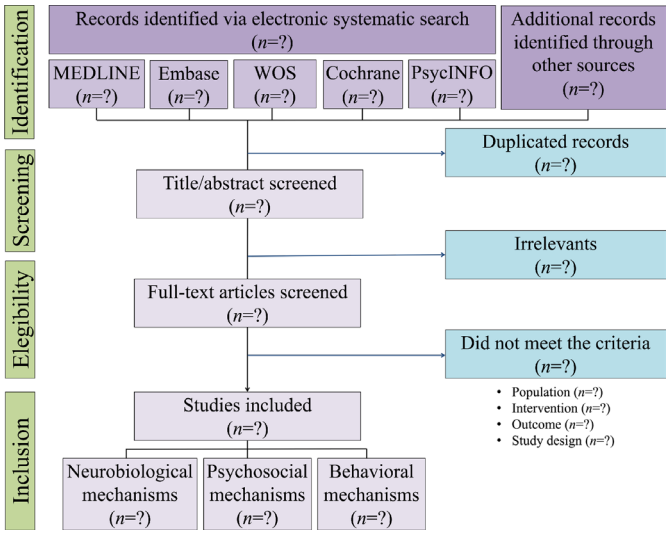

Figure 1 Flow diagram for study selection. WOS, Web of Science.

Population

We will include human studies including participants of all ages. Studies including individuals with physical or psychological disorders diagnosed by medical records, elite athletes and animals will be excluded.

Intervention

We will include all observational studies, which have explored the mechanisms through which physical activity is associated with psychiatric symptoms. Intervention studies examining the mechanisms through which physical activity affects psychiatric symptoms will be also included. Studies in which physical fitness (ie, capacity to perform physical activity, which refers to a full range of physiological and psychological qualities),[18] or sedentary behaviour (ie, any waking behaviour characterised by an energy expenditure ≤1.5 METs, while in a sitting, reclining or lying posture)[19] are the independent variables instead of physical activity (ie, any bodily movement produced by skeletal muscle that results in energy expenditure)[20] will be excluded. Additionally, multiple health behaviour intervention studies (eg, co-interventions such as a dietary programme combined with physical activity) will be excluded because they preclude drawing conclusions on the isolated effect of physical activity or sedentary behaviour on psychiatric symptoms.

Outcomes

We will include the subscales of internalising (ie, depression, anxiety, somatic symptoms) and externalising (ie, conduct problems, rule-breaking behaviour, attention-deficit/hyperactivity problems) disorders.

Study designs

Intervention studies (randomised controlled trials (RCTs), non-RCTs), prospective longitudinal and cross-sectional studies will be included. We will not include conference proceedings and other types of grey literature since risk of bias for these studies cannot be adequately assessed.[21]

Potential mechanisms

Studies will be included if they explored the role of any potential neurobiological, psychosocial or behavioural mechanisms in the relationship between physical activity and psychiatric symptoms. We will refer to the variables used to explore the potential mechanisms as 'mediating variables', but we will include any study exploring the mechanisms linking physical activity and psychiatric symptoms and not only those that used a mediation analysis.

Further restrictions

No language and publication date restriction will be applied. All databases will be searched from their date of inception, and we will include every study that meets the above-mentioned criteria regardless of the language.

Search strategy for identifying relevant studies

With the assistance of a biomedical information specialist, we will develop a systematic search strategy based on the predetermined research question in the following electronic databases: MEDLINE Ovid, Embase.com, Web of Science Core Collection, Cochrane CENTRAL register of Trials and PsycINFO Ovid. First, we will search for potentially relevant studies based on a search strategy that is the combination of Medical Subject Headings terms for Medline and Emtree terms for Embase and free text search. Our research team, including a librarian who is specialised in search strategy development, has developed this search strategy. Search terms are personalised to each database (see online supplemental appendix). Search terms include four parts: (1) terms to identify our independent variable (ie, physical activity); (2) terms to identify our mechanisms (ie, neurobiological, psychosocial, behavioural mechanisms); (3) terms to identify our outcome (ie, psychiatric symptoms) and (4) terms to exclude articles that match our exclusion criteria. An additional search for studies will be performed by screening reference lists of included studies and their citations through Google Scholar. Third, we will contact experts in the field to identify additional studies that may have been missed and any relevant ongoing or unpublished studies.

Study records

Data management

First, we will extract all studies identified by the different sources into an EndNote Library. Second, we will use a published method that uses this software to automatically eliminate the duplicate studies.[22] In our final report, we will note the number of duplicates in the PRISMA flow diagram (figure 1).

Selection process

First, two independent researchers (PTNH and TPBH) will screen titles and the abstracts for eligibility. When disagreements emerge between the two independent

Table 2 Summary of research investigating the mechanisms linking physical activity with psychiatric symptoms (n=?)

Authors, year (country)	N sample (mean age±SD, % females)	Design; target population	Independent variable *(instrument)*	Mediating variable *(instrument)*	Dependent variable *(instrument)*	Statistical analysis; software	Confounders	Main findings

researchers, consensus will be obtained through discussion or when required, the opinion of a third researcher (MR-A) will be considered. Second, we will then obtain the full-text reports of studies that may fit eligibility criteria based on this assessment. Afterwards, the same two independent researchers (PTNH and TPBH) will assess eligibility based on the full texts. Any discrepancies will be again resolved after discussion with a third researcher (MR-A).

Data extraction process

Two researchers (PTNH and TT) will independently extract data from the included studies to a customised data extraction form developed a priori that has been piloted using one eligible study (see table 2). Again, any discrepancies will be resolved after discussion with a third researcher (MR-A). We will contact authors for any relevant missing data.

From eligible studies, we will extract the following items: study background (name of the first author, year and study location), sample characteristics (number of participants, age of participants and percentage of female participants), design (intervention (RCT or non-RCT) or observational (cross-sectional or longitudinal)), independent variables, dependent variables, mediating variables, instruments used to assess the variables, statistical analyses and software, confounders and main findings. For intervention studies (RCTs and non-RCTs), we also extract weeks of intervention, description of the programme, intensity, duration and frequency. For longitudinal studies, we also extract years of follow-up.

Risk of bias and quality of the evidence

The risk of bias will be evaluated independently by two researchers (PTNH and TT) and disagreements were solved in a consensus meeting with the same third researcher (MR-A). The risk of bias will be evaluated using the Joanna Briggs Institute Critical Appraisal Tool for Systematic Reviews (https://jbi.global/critical-appraisal-tools). This tool has already been used by other authors in the field.[23 24] In brief, this tool includes four specific checklists depending on the study design (ie, cross-sectional studies, longitudinal studies, RCTs and non-RCTs). There are four possible answers for each category: 'yes' (criterion met), 'no' (criterion not met), 'unclear' or 'not applicable'. The specific tools include: 8 items for cross-sectional studies, 11 items for longitudinal studies, 9 items for non-RCTs and 13 items for RCTs. Studies will be categorised as 'high risk' or 'low risk'. Specifically, the studies will be considered as 'low risk' if at least 75% of the applicable items are scored as 'yes' (criterion met). In contrast, articles will be considered 'high risk' when <75% of the applicable items were scored as 'yes'. This classification has been previously employed by Molina-Garcia *et al*.[25]

Lastly, the Grading of Recommendations Assessment, Development and Evaluation framework will be used to assess the quality of the evidence across studies.

Data synthesis and analysis

In case overlapping populations are analysed in multiple studies, we will include according to the following hierarchy the study that (1) has the lowest risk of bias, or (2) incorporates the largest sample size. In the case when a study reports multiple effect estimates for overlapping populations, we will select according to the following hierarchy: (1) the most adjusted model, (2) the closest time-point to the end of the intervention or (3) the largest treatment group. Findings from observational and intervention studies will be rated using the method first employed by Sallis *et al*,[26] and more recently by Lubans *et al*[12] and Rodriguez-Ayllon *et al*.[9] If 0%–33% of studies reported a statistically significant mediation (eg, self-esteem) between the independent (eg, physical activity) and dependent variable (eg, depressive symptoms), the result will be classified as no association (Ø); if 34%–59% of studies reported a significant mediation, or if fewer than four studies reported on the outcome, the result will be classified as being inconsistent/uncertain (?) and if ≥60% of studies found a statistically significant mediation, the result will be classified as significant (✓).

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Contributors MR-A, PTNH designed and drafted the protocol. WMB performed the search strategy. MR-A, PTNH, TPBH, TT, AH, DRL and MV revised and approved the final version of the manuscript. MR-A will be the guarantor of the review.

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REFERENCES

1 Pine DS, Cohen E, Cohen P, *et al*. Adolescent depressive symptoms as predictors of adult depression: moodiness or mood disorder? *Am J Psychiatry* 1999;156:133–5.
2 Walker ER, McGee RE, Druss BG. Mortality in mental disorders and global disease burden implications. *JAMA Psychiatry* 2015;72:334–41.
3 Guan B, Deng Y, Cohen P, *et al*. Relative impact of axis I mental disorders on quality of life among adults in the community. *J Affect Disord* 2011;131:293–8.
4 Achenbach TM, Ivanova MY, Rescorla LA, *et al*. Internalizing/Externalizing problems: review and recommendations for clinical and research applications. *J Am Acad Child Adolesc Psychiatry* 2016;55:647–56.
5 Patel V, Flisher AJ, Hetrick S, *et al*. Mental health of young people: a global public-health challenge. *Lancet* 2007;369:1302–13.
6 Dagnino P, Ugarte MJ, Morales F, *et al*. Risk factors for adult depression: adverse childhood experiences and personality functioning. *Front Psychol* 2020;11:3224.
7 Biddle SJH, Asare M. Physical activity and mental health in children and adolescents: a review of reviews. *Br J Sports Med* 2011;45:886–95.
8 Biddle SJH, Ciaccioni S, Thomas G. Physical activity and mental health in children and adolescents: an updated review of reviews and an analysis of causality. *Psychology of Sport and Exercise* 2018:1–10.
9 Rodriguez-Ayllon M, Cadenas-Sánchez C, Estévez-López F. Role of physical activity and sedentary behavior in the mental health of preschoolers. *Children and Adolescents: A Systematic Review and Meta-Analysis. Sports Medicine* 2019.
10 Schuch FB, Vancampfort D, Firth J, *et al*. Physical activity and incident depression: a meta-analysis of prospective cohort studies. *Am J Psychiatry* 2018;175:631–48.
11 Choi KW, Chen C-Y, Stein MB, *et al*. Assessment of bidirectional relationships between physical activity and depression among adults: a 2-Sample Mendelian randomization study. *JAMA Psychiatry* 2019;76:399–408.
12 Lubans D, Richards J, Hillman C, *et al*. Physical activity for cognitive and mental health in youth: a systematic review of mechanisms. *Pediatrics* 2016;138:e20161642.
13 Stillman CM, Esteban-Cornejo I, Brown B, *et al*. Effects of exercise on brain and cognition across age groups and health states. *Trends Neurosci* 2020;43:533–43.
14 Kandola A, Ashdown-Franks G, Hendrikse J, *et al*. Physical activity and depression: towards understanding the antidepressant mechanisms of physical activity. *Neurosci Biobehav Rev* 2019;107:525–39.
15 Phillips C, Brain-Derived Neurotrophic Factor. Depression, and physical activity: making the neuroplastic connection. *Neural Plasticity* 2017.
16 Shamseer L, Moher D, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;349:g7647.
17 O'Connor D, Green S, Higgins JP. Defining the Review Question and Developing Criteria for Including Studies. *Cochrane Handbook for Systematic Reviews of Interventions*. *Chichester, UK: John Wiley & Sons, Ltd* 2008:81–94.
18 Ortega FB, Ruiz JR, Castillo MJ, *et al*. Physical fitness in childhood and adolescence: a powerful marker of health. *Int J Obes* 2008;32:1–11.
19 Tremblay MS, Aubert S, Barnes JD, *et al*. Sedentary Behavior Research Network (SBRN) - Terminology Consensus Project process and outcome. *Int J Behav Nutr Phys Act* 2017;14:75.
20 Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. *Public Health Rep* 1985;100:126–31.
21 Kho ME, Eva KW, Cook DJ, *et al*. The completeness of reporting (core) index identifies important deficiencies in observational study conference Abstracts. *J Clin Epidemiol* 2008;61:1241–9.
22 Bramer WM, Giustini D, de Jonge GB, *et al*. De-duplication of database search results for systematic reviews in endnote. *J Med Libr Assoc* 2016;104:240–3.
23 Haynes A, Kersbergen I, Sutin A, *et al*. A systematic review of the relationship between weight status perceptions and weight loss attempts, strategies, behaviours and outcomes. *Obes Rev* 2018;19:347–63.
24 van Ekris E, Altenburg TM, Singh AS, *et al*. An evidence-update on the prospective relationship between childhood sedentary behaviour and biomedical health indicators: a systematic review and meta-analysis. *Obes Rev* 2016;17:833–49.
25 Molina-Garcia P, Migueles JH, Cadenas-Sanchez C, *et al*. A systematic review on biomechanical characteristics of walking in children and adolescents with overweight/obesity: possible implications for the development of musculoskeletal disorders. *Obes Rev* 2019;20:1033–44.
26 Sallis JF, Prochaska JJ, Taylor WC. A review of correlates of physical activity of children and adolescents. *Med Sci Sports Exerc* 2000;32:963–75.