

Physical activity and endogenous pain modulation in older people: a scoping review protocol

Debora Verbelen¹ • Natalya Korogod² • Emmanuelle Opsommer^{2,3}

¹University of Applied Sciences and Arts Western Switzerland (HES-SO) and University of Lausanne (UNIL), Lausanne, Switzerland, ²School of Health Sciences (HESAV), University of Applied Sciences and Arts Western Switzerland (HES-SO), Lausanne, Switzerland, and ³Bureau d'Echanges des Savoirs pour des pratiques Exemplaires de Soins (BEST): A JBI Centre of Excellence, Lausanne, Switzerland

ABSTRACT

Objective: This scoping review aims to provide an overview of the existing literature on physical activity and endogenous pain modulation (EPM), assessed using conditioned pain modulation (CPM), with a specific focus on older people with chronic pain.

Introduction: Approximately 20% of the European population reports chronic pain, highlighting the problem of chronic pain in the general population. This prevalence increases to 50% in older people. Physical activity is one of the most frequently used treatments for pain management and relief. A possible mechanism underlying the positive effects of physical activity on pain may be related to its influence on EPM. The review will map i) types of physical activity used to study its effect on EPM in older people; ii) intervention protocols investigating physical activity and EPM, measured using CPM, in older people experiencing pain; and iii) knowledge gaps requiring further research or interventions adapted to older people with pain.

Inclusion criteria: This review will consider studies of people aged 60 years or older, using CPM to examine the effect of physical activity on EPM. All types of care settings will be eligible.

Methods: This review will be conducted in accordance with the JBI methodology for scoping reviews. The following databases will be searched: MEDLINE (Ovid), CINAHL (EBSCOhost), Embase, Cochrane Library, Web of Science, *JBI Evidence Synthesis*, PsycINFO, and PEDro.

Review registration: Open Science Framework <https://osf.io/e7ndy/>

Keywords: endogenous pain modulation; exercise; older people; physical activity; scoping review

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Introduction

Approximately 20% of the European population reports chronic pain, which highlights the problem of chronic pain in the general population.¹ However, the prevalence of chronic pain exceeds 50% in community-dwelling older adults and 80% in nursing home residents.² Given that the number of older adults is increasing each year, predictions indicate that by 2050, 30% of the European population will be aged 65 years or older.³ Currently, chronic pain in older adults already affects society due to the associated costs and the impact on the individual's

health and quality of life.⁴ Chronic pain is also associated with limitations in activities of daily living and can lead to social isolation, increased fall risk, increased risk of cognitive impairment, and accelerated frailty.^{1,5} Coping with chronic pain is not easy and is often linked with negative experiences if adjustments to daily life activities are necessary. Many individuals living with chronic pain are pessimistic about their prognosis and feel they are burdening their families.⁶

The treatment of chronic pain can be either pharmacological or non-pharmacological, or it can involve multimodal, interdisciplinary treatment.⁷ Pharmacological treatment is not without risk in older people because of possible side effects, polypharmacy, and addictions.⁸ Therefore, non-pharmacological treatments are preferable because they involve little to no

Correspondence: Emmanuelle Opsommer, emmanuelle.opsommer@hesav.ch

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harmful side effects. One of the most frequently recommended treatment strategies to manage pain is physical activity, which is already commonly used in clinical practice to improve pain severity and physical function.⁹ In a review by Geneen *et al.*,¹⁰ exercise was linked to reduced pain severity in patients with chronic pain; however, the evidence was rather limited. Reasons for this limited evidence can be linked to the broad range of interventions that were examined, including mobility, strength, endurance, as well as the heterogeneity between studies in terms of samples, methods, and analysis.¹⁰ Although evidence of exercise in patients with chronic pain is rather limited, physical activity and supervised group exercise programs, including cardiovascular, mind-body, strength, or a composite thereof, were included in the chronic pain guidelines published by the UK National Institute for Health and Care Excellence (NICE).⁷ These guidelines recommend a combination of psychological therapies, physical activity, and exercise to change behavior toward greater participation and improved quality of life.⁷ This reflects the strong belief in physical activity as a treatment for chronic pain; however, knowledge of the underlying mechanisms as well as adapted protocols for exercise prescription and physical therapy are lacking.

A possible mechanism underlying the positive effects of physical activity on pain may be related to its influence on endogenous pain modulation (EPM).^{11,12} EPM is a comprehensive concept that encompasses the array of mechanisms through which the central nervous system modulates pain perception.¹³ It is a general term that includes actions of the central nervous system to either inhibit or facilitate pain. It was first described by Le Bars *et al.*¹⁴ in 1979 through the term *diffuse noxious inhibitory control* (DNIC). This paradigm, tested on rats, showed that ongoing pain can be inhibited by introducing new pain in a remote area. The authors found that by adding a painful stimulus, the activity of convergent dorsal horn neurons changed in a spino-bulbo-spinal loop.¹⁴ This study showcased how the modulation of pain signals can occur through complex interactions within the central nervous system, offering a vivid illustration of the concept of EPM. It is pertinent to acknowledge that this pain inhibitor–pain mechanism is also recognized as a crucial process within the human body’s pain modulation system.¹⁵ Importantly, it closely aligns with the descending pain inhibitory pathway, a network in the nervous system responsible for

reducing the intensity of pain signals as they travel from their source to the brain.¹⁶ This connection suggests that activating the descending pain inhibitory pathway eases pain signals, resulting in a natural pain relief effect.¹⁶ Both the descending and ascending pain inhibitory pathways are distinct mechanisms that contribute to the modulation of pain signals, and together, they constitute pieces of the broader puzzle of EPM.^{13,17} Insights into the dynamics of the descending pain inhibitory pathway in humans and its connection to EPM can be obtained through conditioned pain modulation (CPM).¹⁶

CPM is a psychosocial experimental measure of the net effect of the descending pain pathway.¹⁶ The CPM paradigm involves applying a secondary painful stimulus (conditioning stimulus or CS) after an initial painful stimulus (test stimulus or TS).¹³ In practice, pain intensity is evaluated after exposure to a painful TS, which will, in most cases, reduce immediately after exposure to CS. Therefore, the addition of CS facilitates the descending inhibitory pathway in most cases. However, in a few cases, the pain intensity may be augmented by adding CS, which means that the descending inhibitory pathway is inhibited.¹⁶ For instance, research has shown that CPM is impaired in patients with chronic pain, indicating compromised EPM mechanisms.¹⁸ Similarly, impaired CPM responses were also observed in older adults.¹¹ This aligns with parallel outcomes discovered in alternate studies utilizing diverse methodologies to evaluate EPM.^{19,20} Both age and chronic pain seem to influence EPM, possibly explaining the high prevalence of chronic pain in older adults.¹² This effect may impede the process leading to central sensitization and prevent the development or maintenance of chronic pain.¹¹ In contrast, exercise positively affects CPM by adjusting the complex network of pathways involved in pain processing.¹¹ As already mentioned, when exposed to a painful TS followed by a secondary painful CS, the descending pain pathway’s activity is modulated. Engaging in regular vigorous exercise amplifies this modulation, measured using CPM, by adjusting the balance of excitatory and inhibitory transmission in the ascending and descending pain pathways.^{11,21} Other potential mechanisms that could explain the beneficial effects of physical activity on EPM include alterations in neurotransmitters of the central nervous system, increased endogenous opioids, and preservation of brain structures that are critical to the functioning of EPM.¹¹

Although physical activity seems to be a promising treatment with little to no harmful side-effects, it is still not clear how it should be adapted to older people suffering from both acute and chronic pain. This scoping review aims to identify current evidence about physical activity and EPM, assessed using CPM, with a specific focus on older people with pain.

A preliminary search of MEDLINE, the Cochrane Database of Systematic Reviews, and *JBIEvidence Synthesis* was conducted, and no current or in-progress systematic reviews or scoping reviews on the topic were identified.

Review questions

- i) What types of physical activity are used to study its effect on EPM in older people?
- ii) What intervention protocols are used to investigate physical activity and EPM, measured using CPM, in older people experiencing pain?
- iii) Are there knowledge gaps requiring further research or interventions adapted to older people with pain?

Inclusion criteria

Participants

This scoping review will consider all people aged 60 years or older with both acute and chronic pain. The World Health Organization indicates that common health conditions are associated with aging, as well as the emergence of several complex health states that correspond to the targeted population of this scoping review.²²

Concept

The overarching concept of interest in this scoping review is physical activity as an intervention because it may relieve pain and seems to have a positive influence on EPM.³ Physical activity can be defined as “people moving, acting, and performing within culturally specific spaces and contexts, and influenced by a unique array of interests, emotions, ideas, instructions, and relationships.”^{23(p.5)} We will include physical activity interventions as planned, structured, and repetitive bodily movements with the objective of improving or maintaining physical fitness.²⁴ Therefore, the review will include studies that use physical activity and CPM to assess the (in)efficacy of EPM in older people with pain. All types of physical activity will be analyzed in terms of frequency, duration, intensity, and/or mode.

Context

Studies in all types of care settings will be eligible (acute care, inpatient rehabilitation, outpatient rehabilitation, and chronic care) in any country. Although the term CPM was first introduced in 2010, studies will be included from the year 2000 onward.²⁵ Before 2010, other terms, such as DNIC, counterirritation, and heterotopic noxious counter stimulation, were used. To ensure relevance to current practice, studies will be limited to the year 2000 and onward.

Types of sources

This scoping review will consider quantitative and mixed method study designs for inclusion.

Methods

The proposed review will be conducted in accordance with the JBI methodology for scoping reviews²⁶ and in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR).²⁷

Search strategy

A 3-step search strategy will be used to locate both published and unpublished studies. An initial limited search of MEDLINE (Ovid) and CINAHL (EBSCOhost) was undertaken, followed by an analysis of the text words contained in the titles and abstracts, and of the index terms used to describe the article. A second search using all identified keywords and index terms will then be undertaken across all included databases. Third, the reference lists of all identified reports and articles will be searched for additional studies.

The following databases will be searched: MEDLINE (Ovid), CINAHL (EBSCOhost), Embase, Cochrane Library, Web of Science, the JBI Evidence-based Practice Database (Ovid), PsycINFO, and PEDro. The main search will be reviewed by an experienced librarian and peer-reviewed by another librarian to ensure that the strategies identify all relevant studies available. A search for unpublished studies and conference proceedings will be conducted to identify additional gray literature. The search will include OpenGrey, ProQuest Dissertations and Theses, DART Europe E-theses Portal, the World Health Organization International Clinical Trials Registry Platform, ClinicalTrials.gov, and BASE (Bielefeld Academic Search Engine). Initial

keywords will include elderly OR old people OR older people OR old patient OR older patient OR pain AND physical activity OR exercise OR physical therapy OR training OR movement AND pain modulation OR hypoalgesia OR modulation of pain OR conditioned pain modulation OR hyperalgesia OR nociception (see Appendix I for a sample search strategy for MEDLINE via Ovid).

Studies published in any language will be included. Any potential sources that are in a language other than English will be initially translated through Google Translate and, if deemed to meet the inclusion criteria, the full text will be professionally translated.

Study selection

Following the search, all identified citations will be collated and uploaded to EndNote v.20 (Clarivate Analytics, PA, USA), and duplicates will be removed. Titles and abstracts will be screened by 2 independent reviewers (DV and NK) to assess them against the inclusion and exclusion criteria using Rayyan (Qatar Computing Research Institute, Doha, Qatar). A pilot test with a random sample of 25 titles from relevant sources will be conducted by 2 reviewers and the team will only start screening when 75% (or greater) agreement is achieved. Potentially relevant papers will be retrieved in full and their citation details imported into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI; JBI, Adelaide, Australia).²⁸ The full text of the selected citations will be assessed in detail against the inclusion criteria by 2 independent reviewers. Reasons for the exclusion of sources of evidence at full text that do not meet the inclusion criteria will be recorded and reported in the scoping review. Any disagreements between the reviewers at each stage of the selection process will be resolved through discussion or with a third reviewer (EO). The results of the search and study inclusion process will be reported in full in the final scoping review and presented in a PRISMA flow diagram.²⁹

Data extraction

Data will be extracted from papers included in the scoping review by 2 independent reviewers using a data extraction tool developed by the reviewers based on the JBI template. Using an Excel spreadsheet (Microsoft, Redmond, USA), we will include the following fields: authors, title, country, aim of the article, data collection methods, population

(age, gender), sample size, intervention type, comparator, and details of frequency, duration, intensity, and/or mode of physical activity, use of CPM, outcomes, and key findings that relate to the review questions.

Key information from the selected studies will be recorded in a charting table, as recommended by the JBI methodology for scoping reviews.²⁹ This charting table will be developed and will include authors, year of publication, origin/country of origin, aims/purpose, design, study population and sample size, type of intervention, duration of intervention, provider of the intervention, methodology, type of outcomes, and key findings related to the scoping review questions.²⁹ The draft extraction tool will be tested beforehand to determine its feasibility. The tool will be modified and revised as necessary during the process of extracting data from each of the included evidence sources. The modifications will be detailed in the scoping review.

Data analysis and presentation

The results will be presented in tables, narrative syntheses, a conceptual diagram, a synthesis matrix, and visual infographics if this aligns with the results. The results will be presented by population, concept, and context (PCC), and data extraction will allow us to describe conceptual categories related to the review questions. If knowledge gaps are found, these will also be described.

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Author contributions

All authors decided on the topic. DV wrote the protocol. All authors contributed critical feedback and helped shape the research. NK and DV developed the search.

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Appendix I: Search strategy

MEDLINE (Ovid)

Search conducted: December 12, 2022

Search	Query	Records retrieved
#1	exp Aged/ or exp geriatrics/ or geriatric nursing/ or geriatric assessment/ or homes for the aged/ or health services for the aged/ or (elderly or "old people" or "older people" or "old" or "old patient*" or "older patient*" or "older adult*" or geriatric* or gerontolog* or "aged care" or "geriatric nursing").ti,ab. or exp Chronic Pain/ or exp back pain/ or (chronic adj3 pain).ti,ab.	4,657,359
#2	exp Physical Therapy Modalities/ or exp Exercise/ or ("physical activit*" or exercis* or "physical therap*" or train* or movement).ti,ab. or (physical adj3 therap*).ti,ab. or (physical adj3 activit*).ti,ab.	1,481,659
#3	("pain modulat*" or "endogenous analges*" or "modulation of pain" or "endogenous pain modulat*" or "pain mechanism*" or (pain adj3 modulation)).ti,a	6943
#4	#1 AND #2 AND #3	345
No limits		345