Abstract

Strategies to improve cognitive aging are highly needed. Among those, promotion of exercise and physical activity appears as one of the most attractive and beneficial interventions. Indeed, results from basic and clinical studies suggest that exercise and physical activity have positive effects on cognition in older persons without cognitive impairment, as well as in those with dementia. Despite inconsistent results, aerobic exercise appears to have the strongest potential to enhance cognition. However, even limited periods of walking (45 minutes, three times a week, over a 6-month period) have also been shown to enhance cognition, particularly executive functions. Changing long-term lifestyle habits in these older persons remains a critical challenge and attractive programs susceptible to gain adherence are needed to succeed in achieving improved cognitive aging.

Keywords:

dementia, exercise, physical activity, cognitive aging

Résumé

Les stratégies pour ralentir le vieillissement cognitif manquent cruellement. Parmi celles-ci, il apparaît que la promotion de l’activité physique soit une des plus attractive et bénéfique. En effet, les résultats d’études fondamentales et cliniques suggèrent un effet positif de l’exercice et l’activité physique sur la cognition des personnes âgées tant sans troubles cognitifs, qu’avec des signes de démence. Malgré des effets inconstants, c’est l’exercice aérobie qui semble avoir le plus grand potentiel pour améliorer la cognition. Toutefois, même des durées limitées de marche (45 minutes, trois fois par semaine sur une période de 6 mois) ont aussi montré des bénéfices, en particuliers sur la fonction exécutive. Il reste que le changement des habitudes de vie des personnes âgées constitue un défi difficile, et il existe un besoin de développement de programmes attractifs pour espérer une adhérence permettant un meilleur vieillissement cognitif.

Mots clés :
démence, exercice, activité physique, vieillissement cognitif
Introduction

In 2013, it was estimated that a new case of dementia appeared worldwide every 5 to 10 seconds, adding to the 47.5 million people already affected [1]. According to these projections, the worldwide prevalence of dementia is expected to rise to about 75.6 million by 2030 and 135.5 million by 2050. Cognitive decline and dementia are among the strongest drivers of disease burden and overall health care costs. Strategies to maintain or even improve cognitive aging are therefore highly needed, even though recent data on dementia incidence suggests that these projections might be somewhat modified [2].

Cognitive decline and dementia occurrence relates to the interplay between risk and protective factors. Among the latter, physical activity appears to be one of the most efficient interventions supported by observational as well as interventional data. Indeed, multiples studies in middle-aged and older adults reported benefits from physical activity and exercise in reducing the risk of cardio-vascular events, falls and fractures, depression, as well as functional decline and dependency [3]. As such, physical activity appears as the most important modifiable lifestyle habit that can reduce the morbidity associated with aging. More specifically, recent studies also suggest that physical activity can enhance cognition in older people without dementia and, to some extent, reduce or delay the incidence of dementia. This article reviews the biological and clinical evidence supporting exercise and physical activity as a protective factor to maintaining cognitive performance and healthy cognitive aging, as well as to improving cognition among older persons with dementia.

Evidence from basic research

Numerous studies in animal models, mostly rodents, suggest that exercise improves cognitive-related tasks, in particular memory-dependent tasks. Physical activity may directly and indirectly modulate the formation of beta-amyloid protein through several mechanisms. Strong evidence suggests that physical activity improves cerebral perfusion, stimulates angiogenesis, and regulates inflammatory pathway and growth factor signaling in animal as well as in human studies [4] [5]. In particular, physical activity appears to increase production of the brain-derived neurotrophic factor (BDNF), a growth factor that plays a critical role in cell genesis and brain neuroplasticity [6]. Indeed, aerobic exercise has been specifically shown to improve cognitive performance in rodents and, when sustained, to increase hippocampal neurogenesis, whereas resistance training did not [7]. Neuroimaging studies in human further support these observations in showing larger hippocampal volume among older individuals with higher aerobic fitness [8].

Overall, these studies strongly suggest that physical activity has both indirect (notably through improvement in cerebrovascular and cardiovascular risk factors) and direct (through neurogenesis and increased neuroplasticity as well as cognitive reserve) beneficial effects (Figure 1).

Evidence from observational studies

Initial evidence about the benefits of physical activity on cognition came from observational studies, mostly prospective longitudinal cohort studies. As for any observational studies, those are very sensitive to important and relevant biases. In particular, participants who are physically active are more likely to also adopt other healthy lifestyle habits that might influence the risk of cognitive decline and/or dementia incidence. In addition, older persons experiencing early signs of cognitive decline might also be less likely to remain physically active. To address this potential bias, good-quality observational studies excluded participants who developed cognitive decline and/or dementia over the first years of follow-up and still reported beneficial effects of physical activity on cognition.

A systematic review of prospective studies summarized the observational evidence about the effect of physical activity on cognitive decline in non-demented older persons [9]. A total of 15 prospective studies totaling 33,816 persons aged 65 years and over were followed for up to 12 years (mean duration 5 years). Results showed an overall beneficial effect in preventing cognitive decline that differed only slightly by intensity level (low-to-moderate vs high) of physical activity (Figure 2). Indeed, participants with low-to-moderate and high level of physical activity had decreased probability of
cognitive decline at follow-up by 35% (hazard ratio (HR) 0.65, 95%CI 0.57–0.75) and 38% (HR 0.62, 95%CI 0.54–0.70), respectively, as compared to sedentary participants. Sensitivity analyses showed that smaller studies that included mostly women and had shorter follow-up tended to overestimate the beneficial effect of physical activity. A more recent prospective cohort study in 1228 older persons (mean age 70.6±9.0 years, 60.9% women, 9.6±5.1 years of education) also showed that, among participants without cognitive impairment at baseline, those sedentary or with only low physical activity had a greater decline in episodic memory 5 years later compared to participants with moderate-heavy physical activity. The magnitude of this decline was equivalent to the decline expected over about 10 years of cognitive aging [10].

Another systematic review of prospective studies investigated more specifically the relationship between physical activity and the risk of neurodegenerative disease, including Alzheimer’s disease. Sixteen prospective studies were included that included 163 797 non-demented participants, with follow-up ranging from 3 to 21 years [11]. Results showed that, compared to participants with the lowest level of physical activity, those with highest level had 28% (95%CI 0.60–0.86) and 45% (95%CI 0.36–0.84) lower probability of dementia and Alzheimer’s disease, respectively (Figure 3).

Additional recent studies reported further observational evidence supporting the protective effect of physical activity in young adults for early onset dementia [12], as well as in middle-aged adults for late-life dementia [13].

Evidence from interventional studies

Evidence from interventional studies that investigated the role of physical activity in preventing or delaying cognitive decline in cognitively intact older persons is less consistent. Indeed, numerous systematic reviews and meta-analyses have been performed that reached different conclusions. A 2008 Cochrane systematic review investigated the effect on cognitive performance of physical activity programs that aimed at improving cardio-respiratory fitness in healthy older persons [14]. Aerobic exercise programs resulted in significant improvements in motor function, auditory attention and, to a lesser extent, cognitive speed and visual attention. Another systematic review published in 2010 that included 29 studies of aerobic exercise in 2049 participants reached similar conclusions in showing modest but statistically significant improvements in attention, processing speed, executive function, and, to a lesser extent, memory [15]. A more recent meta-analysis of randomized controlled trials that examined the impact of aerobic exercise, resistance training, and Tai Chi on cognition in older persons without known cognitive impairment provided more mixed results [16]. Whereas significant improvement were observed in reasoning (resistance training), as well as attention and processing speed (Tai Chi), no significant effect was observed from aerobic exercise in any cognitive domain (immediate and delayed recall, working memory, attention, and processing speed). Interestingly, another systematic review and meta-analysis that focused on the effect of walking on executive functions showed that set-shifting and inhibition were both improved in trials that included sedentary older people without cognitive impairment, whereas walking did not improve any executive task among cognitively impaired older persons [17]. In this review, some studies that showed benefits used limited walking periods, such as 45 minutes, three times a week, over 6 months. This appears extremely attractive in terms of program adherence.

In contrast, an updated 2015 Cochrane review concluded to the absence of any cognitive benefits of aerobic exercise on cognition in healthy older persons, even when analyses were restricted to programs that succeeded in improving cardio-respiratory fitness [18].

Overall, the heterogeneity of these results probably reflects important variations in the type of population enrolled in these trials as well as differences in cognitive tests used as outcomes (i.e., general measure of overall cognition, such as the mini mental state exam, or specific cognitive function, such as executive tests). Moreover, exercise program components, duration, and intensity, as well as participants’ adherence also vary across trials.

Despite these limitations, overall evidence still suggests that interventions that promote physical activity, enhance endurance, and increase strength might provide cognitive benefits in cognitively intact older persons, especially in executive functions. Questions remain about the most efficient type of activity (aerobic vs resistance training vs combined) to maximize benefits, and recent evidence support the empiric recommendation to combine activities in multi-component exercise programs [19]. Moreover, the effectiveness of such exercise programs would likely be further enhanced if combined with interventions in other domains such as diet, cognitive training, and vascular risk factors control, as recently shown [19]. Nevertheless, evidence supporting the effectiveness of simple interventions such as walking on preserving executive functions is especially encouraging. In older persons, recommendations to increase walking are more realistic to implement in the real-world than more ambitious multifaceted interventions targeting lifestyle and habits [20].

![Image](image.png)

**Figure 3:** Results from observational studies showing the risk reduction in overall dementia and Alzheimer’s disease, respectively, in participants with the highest level of physical activity over the follow-up period (ranging from 3 to 21 years). Participants with lowest level of physical activity used as reference group (from ref [11]).

**Physical activity in persons with dementia**

This review would not be complete without briefly discussing the role of physical activity in persons with dementia. Indeed, pharmacological treatments currently available have only modest, symptomatic, effects, but do not alter the course of...
dementia and may have side effects. Physical activity therefore also attracted attention as a potential intervention to incorporate into the management of patients with dementia. However, a discussion of the role and effects of exercise and physical activity in the management of all dementia manifestations (in particular for behavioral and psychological symptoms of dementia) is beyond the scope of this paper. This section will therefore focus on the specific effect of physical activity on cognitive function in these patients. A meta-analysis of 18 randomized controlled studies assessed the effect on cognition of aerobic-only, non-aerobic, and combined (aerobic and non-aerobic) programs of physical activity in a total of 802 patients (mean age about 80 years, 68% women), most with Alzheimer’s disease [21]. Results showed a positive effect on cognitive function that was not modified by age and/or disease severity, or dementia type. Aerobic-only and combined interventions (but not non-aerobic) had similar positive effects on cognition, whereas variations in programs’ intensity (high vs low frequency) did not modify effectiveness.

Although the underlying mechanisms explaining these encouraging results remain putative (neurotrophin level enhancement, neurogenesis, improved vascularization, etc.), these results strongly support the inclusion of physical activity as a component of dementia management programs.

Conclusions

Physical activity appears as a potential key factor to enhance cognitive aging. Basic as well as clinical data from observational studies and interventional trials strongly suggest that exercise and physical activity have positive effects on cognition, particularly executive functions and attention in older persons without cognitive impairment. Moreover, benefits of physical activity are also apparent among older patients with dementia, even though evidence is weaker. Although aerobic exercise appears to have the strongest potential to enhance cognition, some evidence also supports walking as a simple, easy to adhere to, and cost-effective intervention. Indeed, a critical question would be to propose attractive programs to gain adherence among older persons and achieve significant changes in lifestyle habits in order to enhance cognitive aging and thus address the formidable challenge of dementia epidemics.

Practical implications

- Regular physical activity and exercise are important contributors to healthy cognitive aging.
- Lifelong physical activity probably offers the best protection to maintain cognitive performance, some evidence suggest that starting to exercise at older age might still provide significant cognitive benefits.
- Aerobic exercise and resistance training interventions appear to be the most effective type of exercise to enhance cognitive performance in persons without as well as in those with dementia.
- Walking 45 minutes three times a week has also been shown to provide benefits in executive functioning and might therefore be a realistic recommendation in sedentary older persons to enhance their cognitive aging.

Acknowledgments and conflict of interest

The author declares no conflict of interest in relation to this article.

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