Physical Activity and Its Prophylactic Effects on Cognition and Dementia

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Abstract

The dynamics of aging are not identical for all individuals, and certain lifestyle factors are likely to modulate its effects. Among these factors, the regular practice of physical activity is now the subject of increasing research. Many epidemiological, cross-sectional, and interventional studies present a convincing body of evidence in favor of the prophylactic effect of regular physical activity on brain and cognitive health in older adults. Various cognitive functions such as information processing speed, executive functions, or declarative memory appear to function more efficiently under the effect of a 6-month program combining 45 minutes of moderate-to-high-intensity aerobic physical exercise (sustained walking, jogging) and strength training three or more times a week.

Introduction

The world’s population is currently aging, with 900 million people aged 60 and over worldwide [1]. The prevalence of dementia and Alzheimer’s disease (AD) is consequently on the rise. The number of people with dementia worldwide has been estimated at 50 million in 2019, a figure set to almost double every 20 years, reaching 152 million by 2050 [2]. Dementia and AD are recognized public health problems in high-income countries, where national plans are gradually being put in place, encouraged by the World Health Organization (WHO). The human, social, and economic consequences are considerable, with increased mortality among the elderly and a loss of autonomy for sufferers requiring assistance and medical care. AD represents a global challenge for the 21st century [3]. Age-related cognitive decline is thought to be particularly pronounced for tasks requiring information processing speed, as well as for tasks requiring the use of working memory and executive control processes. Unfortunately, there is no disease-modifying treatment for dementia.

Epidemiological research can therefore highlight modifiable targets for prevention [4]. Physical activity is a promising target [5]. It has been estimated that 3% of dementia cases could be prevented by increasing levels of physical activity in everyday life [6-8], and a growing body of literature points to the importance of physical activity (any bodily movement produced by skeletal muscle that results in energy expenditure) and exercise (a subset of planned, structured, and repetitive physical activities) in preventing and slowing pathological processes and problems associated with dementia [9]. In this respect, older people who are physically active are more likely to retain their cognitive faculties than those who are not [6].

The important role of physical activity has also been highlighted for people already living with dementia. Indeed, physical exercise helps to improve important outcomes, such as cognition [10]. In addition, physical activity in general and exercise interventions in particular could help to improve the behavioral and psychological symptoms of dementia [11].

With demographic aging on the increase in Algeria, we need to look at all the means at our disposal to prolong the autonomy of senior citizens, and physical activity is one of the possible preventive strategies. However, a clear distinction needs to be made between the acute and chronic effects of exercise on cognition.
Acute effects of physical exercise refer to the immediate, or short-term, effects of a single period of physical activity of limited duration (from a few seconds to a few hours); for example, the effects of isometric contraction of the forearm muscles at 70% of maximum force for 30 seconds on the subject’s mood or the effects of completing a 45-minute jog at 70% of reserve heart rate (RHR) on the efficiency of decision-making processes measured during or immediately after exercise. The acute effects of exercise are transient, meaning that they begin to operate shortly after the onset of exercise and cease seconds or minutes after the physical activity has ceased. These effects are generally considered to temporarily modulate the electrochemical activity of the neural networks that make up the central nervous system [12]. The chronic effects of physical exercise concern the long-term effects of a 6-week stretching program on postural balance or those of a Nordic walking program, which can last from a few weeks to several years, on cerebral plasticity and the efficiency of cognitive functions; for example, the effects of a 9-month program on episodic memory. The chronic effects of exercise are considered to be long-lasting effects that modify the anatomy of the brain’s connectivity or vascularization networks. We present evidence of the benefits of physical exercise on cognition and on the prevention of cognitive decline.

**Convincing Arguments in Favor of the Benefits of Physical Activity on Cognition and Brain Health**

Several longitudinal and epidemiological studies carried out in North America and Europe between the end of the 20th and the beginning of the 21st centuries have shown that physical activity reduces the risk of neurodegenerative diseases (Alzheimer’s disease) and slows down the deleterious effects of age on cognitive functions.

**The ACT (Adult Changes in Thought) study** [13], carried out in the USA between 1994 and 2003 in the Seattle area on a population of 1,740 people aged over 65 who were in good cognitive health at the start of the study, showed that the rate of dementia was lower in people who took part in physical activity three or more times a week (13 per 1,000 person-years) than in those who took part less than three times a week (19.7 per 1,000 person-years).

In a similar vein, **the CSHA (Canadian Study of Health and Aging) study** [14], carried out in Canada on a sample of 4,615 people aged over 65 in 1991 and 1992 and again in 1996 and 1997, showed that regular physical activity could be considered a protective factor against Alzheimer’s disease, with an odds ratio of 0.69, or 31% less risk of developing the disease.

**The FINE (Finland, Italy, and the Netherlands Elderly) study** [15], carried out over a 10-year period between 1990 and 2000 in three European countries, showed that the cognitive functions of 295 people aged over 70, assessed using the Mini Mental State Examination (MMSE), declined significantly in people who reduced their daily volume of physical activity, whereas they remained stable in participants who increased it.

**The Zutphen Elderly Study (ZES)** [16], a longitudinal study carried out in a town in eastern Holland in 1990 and again in 1993 on 347 people aged 65 to 84, showed very similar results. The relative risk of developing cognitive decline, measured using the MMSE, was twice as high in individuals who engaged in less than 1 hour of physical activity per day as in those with a higher volume of physical activity.

Finally, in the MoVI E (Monongahela Valley Independent Elders Survey) study [17], carried out on 929 people aged over 65 over a 3-year follow-up between 1991 and 1993, or from 1993 to 1996, the relative risk of cognitive decline, again measured using the MMSE, is more than twice lower in individuals who engage in aerobic physical activity lasting more than 30 minutes at least three times a week than in those who do not engage in any physical activity.

Several cross-sectional studies [18-26] have presented convincing arguments in favor of a positive and effective influence of chronic exercise on brain and cognitive aging and have shown that there is a significant positive correlation either between activity or fitness level and brain health as measured by various neurophysiological indicators (brain volume, brain wave amplitude, activation of brain areas), or between activity or fitness level and cognitive performance (speed and/or accuracy of responses), or both.

**Characteristics of Physical Activity Programs with a Positive Effect on Cognitive Functions**

The optimal conditions for obtaining a positive effect of moderate amplitude from exercise on cognitive health are broken down into several parameters:

- **Duration of the physical activity program:**
  For there to be chronic effects likely to modify the anatomy of certain brain structures, sufficient time is needed for these mechanisms to take hold, leading to observable effects at biological and then behavioral levels. The meta-analysis by Colcombe and Kramer [27], based on 18 intervention studies published between 1966 and 2001 and conducted on samples of senior citizens with no central nervous system pathology, shows that programs lasting over 6 months produce the greatest effects ($g = 0.674$).
  Furthermore, it was surprising to note that short programs (1 to 3 months) gave rise to significantly greater effects than medium-length programs (4 to 6 months): $0.522$ vs. $0.269$, respectively. No explanation is given for this paradox, but it is possible that short-term learning and/or motivation phenomena partly explain the greater effects of very short programs.
In any case, it seems that the minimum duration for significant and lasting improvements in cognitive performance is around 3 to 5 months [28, 29]. It is very likely that the minimum duration for observing behavioral effects also depends on the frequency of training sessions. We can assume that the greater the frequency, the shorter the minimum time required to observe positive effects.

- **Frequency of training sessions:**
  There appears to be a dose-response relationship between the amount of physical activity and health. The American College of Sport Medicine recommends at least five 30-minute sessions of moderate-intensity physical activity per week, or five 20-minute sessions of vigorous-intensity activity, or an equivalent combination of the two [30]. As one of the barriers to regular physical activity is the difficulty of taking part in other competing activities (e.g., caring for grandchildren, participating in cultural or leisure activities), it is vital that the physical activity program is not too demanding on the schedule.

- **Exercise intensity:**
  The various physiological mechanisms thought to underpin the beneficial effects of physical activity on brain and cognitive health require moderate-to-vigorous exercise intensity. Generally speaking, exercise intensity is expressed as a percentage of the VO2-max "maximum volume of oxygen" used during incremental exercise or, more practically, as a percentage of maximum heart rate (max HR) or the recovery heart rate (RHR) (RHR = max HR - rest HR).
  According to the American Institute of Sports Medicine, low intensity corresponds to 20-39% of RFC, moderate intensity to 40-59% of RFC, and high intensity to 60-84% of RFC [30]. Exercise intensity must exceed 40% of RFC to bring about a significant improvement in cardio-respiratory and cardiovascular health, thought to be responsible for brain and cognitive health.

- **Duration of training sessions:**
  Colcombe and Kramer’s meta-analysis shows that training sessions lasting 31 to 45 minutes significantly greater effect \( (g = 0.614) \) than those of 46 to 60 minutes \( (g = 0.466) \) and those of 15 to 30 minutes \( (g = 0.176) \). As sedentary elderly people tire relatively quickly, it is advisable not to exceed 60 minutes of training per session.

  In general, training sessions comprise three phases: a preparation phase, a phase of work at the target intensity (the actual body of the session), and a cool-down phase. In view of the above-mentioned factors, training sessions should last a maximum of 60 minutes, with a session body of 30 to 45 minutes.

  However, it has been established that cardiorespiratory benefits are much greater when exercise intensity is individualized and adapted to each person’s abilities [30].

  Colcombe and Kramer’s meta-analysis shows, moreover, that combined programs of aerobic exercise (exercise at intensities ranging from 40 to 85% of RHR with activities such as walking, jogging, cycling, swimming or cross-country skiing, help to develop aerobic capacity and power) and strength training (If you want to do an activity with an intensity of less than 40% of RHR, you'll need to choose stretching, intersegmental coordination and postural balance exercises, body awareness, which can be found in activities such as yoga, tai-chi-chuan, gentle gymnastics, eutonie or the Feldenkrais method, the latter two emphasizing relaxation and muscle tone control, segmental dissociation and/or focusing attention on somaesthetic and kinaesthetic information), give rise to significantly higher effect sizes \( (g = 0.59) \) than programs consisting solely of aerobic exercise \( (g = 0.41) \). This result was confirmed by Smith et al’s meta-analysis [31].

**The Effect of Chronic Exercise on Cognitive Processes**

The positive effect of regular physical activity on cognition is now clearly established by epidemiological, cross-sectional, and interventional studies. Colcombe and Kramer’s meta-analysis [32] was the first to show that not all cognitive functions are affected in the same way. The effect of exercise was significantly greater in executive tasks \( (g = 0.68) \) than in all other types of tasks (attentional, visuospatial, and speed of information processing). The meta-analysis by Angevaren et al. [33], based on 11 interventional studies published between 1989 and 2002 and carried out in senior citizens without central nervous system pathology, which compared the effect of aerobic exercise programs versus no intervention, revealed significant effects of aerobic exercise on visual attention.

In addition, comparisons of the effects of aerobic exercise programs with any other type of intervention (strength training, stretching and postural balance programs, mental training, or social interaction sessions around a variety of themes) showed significant effects of aerobic exercise on cognitive speed and visual attention.

The meta-analysis by Smith et al. [34] of a set of 29 randomized controlled trials carried out on samples of people aged over 18 with or without central nervous system pathology observed a positive effect of chronic exercise on attention, processing speed, executive functions, and declarative memory. The effect on working memory was not significant.

The results of these three meta-analyses lead to radically different conclusions regarding the selectivity of the effects of chronic exercise on cognitive functions. Overall, chronic exercise affects a wide repertoire of cognitive functions. In addition, comparisons of the effects of aerobic exercise programs with any other type of intervention (strength training, stretching and
postural balance programs, mental training, or social interaction sessions around a variety of themes) showed significant effects of aerobic exercise on cognitive speed and visual attention.

**Causal Link between Chronic Physical Exercise and Improved Cognitive Performance**

Five main mechanisms induced by regular physical activity have been evoked in the literature:
- an increase in regional cerebral blood flow in certain cortical areas;
- an increase in synaptic plasticity;
- increased neurogenesis;
- an increase in cerebral catecholamines;
- increased effort invested in cognitive tasks.

- **The increased cerebral blood flow hypothesis**, better known as the circulatory hypothesis [35], is certainly the mechanism most often evoked to explain the positive effect of exercise on cognitive aging. It is considered that chronic aerobic exercise causes an increase in cerebral perfusion and regional blood flow. In the course of non-pathological cerebral aging in humans, there is usually a decrease in cerebral blood flow at rest, a decrease in baseline brain activity, especially in frontal regions, and a decrease in regional cerebral blood flow measured in frontal regions during tasks involving executive control [36, 37]. In patients with Alzheimer’s disease, it is also common to observe cerebrovascular dysfunction caused by cerebral amyloid angiopathy, which participates in regional hypoperfusion, reduced cerebral metabolism, and cognitive decline [38]. A few studies in animals [39] and humans [40] suggest that chronic aerobic exercise increases cerebral perfusion and leads to the appearance of new cerebral capillaries, a phenomenon known as angiogenesis [41]. It therefore seems reasonable to think that cerebral perfusion and cerebral blood flow can be increased in certain brain regions, notably the frontal and parietal areas of the cortex, by regular moderate-to-high intensity physical activity.

- **Synaptic plasticity hypothesis**: This hypothesis considers that, under the effect of new sensory and motor experiences linked to the practice of physical activities, the cerebral connectivity network will modify itself by creating new connections (synaptogenesis) or by reinforcing the efficiency of the synaptic transmission of certain connections.

- **The increased neurogenesis hypothesis** is relatively recent. It has been shown in animals that chronic physical exercise facilitates neurogenesis [41] and that these new neurons manage to integrate into fully functional connectivity networks. With this in mind, Pereira et al. [42] observed neurogenesis in the dentate gyrus of the hippocampus in both mice and humans (young adults) following an exercise program. Increased brain volume was also correlated with improved cardiorespiratory health and cognitive performance (learning tasks). The study by Erickson et al. [43] showed that a 6-month program of aerobic physical activity resulted in a 2% increase in hippocampal volume, associated with improved spatial memory performance. We may assume that this mechanism of hippocampal or neocortical neurogenesis induced by chronic exercise plays a part in improving the cerebral and cognitive health of senior citizens.

- **The cerebral catecholamine hypothesis**, better known as the dopaminergic hypothesis, considers that chronic aerobic exercise induces a cerebral release of catecholamines (dopamine and noradrenaline), leading over time to an increase in central dopaminergic receptors, particularly in the prefrontal regions. Cerebral aging is generally accompanied by a deterioration in dopaminergic pathways. A drop in brain dopamine levels, necessary for the proper functioning of executive functions, has been observed in people with normal brain aging. Various diseases of the central nervous system associated with cerebral aging (Parkinson’s disease, Alzheimer’s disease) are also characterized by an abnormal reduction in dopamine levels in the basal ganglia, associated with cognitive deficits. We also know from human and animal studies that performance on tasks involving prefrontal executive functions is sensitive to brain dopamine levels [44]. Finally, several studies, mainly in animals, show that chronic aerobic exercise increases the number of D2 dopamine receptors in striatal regions and facilitates brain dopamine synthesis [41]. It is therefore quite plausible to envisage that regular aerobic exercise, which is known to induce cerebral catecholamine release, leads over time to a change in the occupancy rate of dopaminergic receptors in different brain regions such as the prefrontal cortex and striatum, and thus to an improvement in cognitive functions strongly underpinned by dopaminergic pathways.

These first four hypotheses are all underpinned by the same molecular mechanism known as the neurotrophic hypothesis. Various animal studies have shown that exercise induces the release of neurotrophic factors that increase brain plasticity, notably by participating in angiogenesis, neurogenesis, synaptogenesis, and neurotransmitter synthesis [41]. The three main neurotrophic factors identified to date are:

- Brain-derived neurotrophic factor (BDNF), a key protein in brain plasticity, learning, and hippocampal neurogenesis;
- Vascular endothelial-derived growth factor (VEGF), a protein whose main role is to stimulate angiogenesis;
- Insulin-like growth factor 1 (IGF-1), a peptide hormone secreted by the liver, stimulates cartilage growth,
crosses the blood-brain barrier, and stimulates neurogenesis and angiogenesis.

- **The increased effort hypothesis differs** from the previous hypotheses in that it uses a psychological mechanism to explain the positive effect of chronic exercise on certain tasks or cognitive functions. This hypothesis considers that individuals confronted with a physical activity program requiring a substantial commitment develop skills and metacognitions in the field of mental effort management. These would then be reinvested when performing cognitive tasks requiring an investment in mental effort.

All the explanatory mechanisms mentioned above are, of course, not exclusive and may well coexist depending on the characteristics of the physical activity program in place.

**Moderators of the positive effects of chronic exercise on cognitive and cerebral aging**

Various factors can attenuate or amplify the supposedly direct relationship between chronic exercise and cerebral and cognitive aging. These factors are commonly referred to as moderators.

- **The first factor is the age of seniors.**

Colcombe and Kramer’s meta-analysis [27] showed that the positive effect of chronic exercise on cognitive aging is significantly greater in middle-aged seniors (66 to 70 years) (g = 0.693) than in old seniors (71 to 80 years) (g = 0.549) or young seniors (55 to 65 years) (g = 0.298). The effect was also significantly greater in older seniors than in younger seniors, particularly for two executive functions: behavioral inhibition and working memory updating. This suggests that the body is more sensitive to the positive effects of exercise from the age of 65 onwards, that this effect lasts well into old age, and that continued physical activity is therefore recommended with advancing age.

- **The second moderator is the gender of senior citizens.**

The meta-analysis by Colcombe and Kramer [27] clearly showed that women are significantly more sensitive to the positive effect of chronic exercise (g = 0.604) than men (g = 0.150). This moderating effect of gender could be explained by the fact that some women undergo estrogen-based hormone replacement therapy after menopause, and that this treatment acts on the intracerebral production of BDNF and magnifies the chronic effect of exercise on brain and cognitive health.

- **The third moderator concerns dietary habits.**

Various studies have shown that diet can specifically influence certain molecular mechanisms involved in cognitive functioning.

For example, a diet rich in omega-3 fatty acids, such as docosahexaenoic acid (DHA) found in oily fish and krill (a type of shrimp found in the Atlantic Ocean), appears to have positive effects on cognitive processes in humans and to interact positively with the effect of exercise on synaptic plasticity [45].

A high dietary intake of fruits, vegetables, and flavonoids, sources of antioxidants, has also been associated with better cognitive performance and a lower risk of Alzheimer’s disease [46]. As physical activity increases oxidative stress, an adequate intake of antioxidant nutrients should potentiate its effects.

- **The fourth moderator concerns the genetic make-up of the subjects.**

**Polymorphism of the APOE gene “Apolipoprotein E”**

Individuals carrying the APOE*4 allele and having a low level of physical activity have been shown to have a higher risk of developing cognitive decline and Alzheimer’s disease in the course of aging. Rovio S. et al. reported that the positive effect of chronic physical exercise on cognition was greater in individuals carrying the APOE*4 genotype [47].

**BDNF gene polymorphism**

The involvement of the BDNF gene is strongly suggested by the neurophysiological mechanisms thought to underlie the positive effect of exercise on brain plasticity. The BDNF gene can possess either a methionine (Met) or valine (Val) allele. Several studies have shown that cognitive performance and brain volume are reduced in Met allele carriers compared with Val homozygotes [48]. It has also been shown that intracerebral BDNF concentration increases significantly with regular physical activity [49], as well as with dietary restriction or diets rich in omega-3 acids. The effects of physical activity could therefore interact with BDNF gene polymorphisms and diet.

**Catechol-O methyl transferase (COMT) gene polymorphism**

COMT is the main enzyme responsible for intracerebral dopamine catabolism, which affects executive function and frontal cortex physiology. Individuals with a Met allele at codon 158 would have low COMT enzyme activity and thus reduced dopamine metabolism, leading to higher local concentrations, while those with a Val allele would have high activity of the same enzyme. Dopamine is a key neurotransmitter in many cognitive functions, such as executive function and episodic memory in the elderly.

The COMT gene would therefore determine cortical dopamine concentration and performance in various cognitive tasks. Several studies using brain imaging in humans confirm this hypothesis. Animal studies have shown that regular physical activity induces an increase in intracerebral dopamine concentration. It is possible that the positive effect of chronic exercise on executive functions varies according to the polymorphism of the COMT gene. The study by Voelcker-Rehage C et al. confirmed the moderating role of this polymorphism on...
the positive influence of physical activity on cognitive health [50].

Cognitive Reserve

The concept of cognitive reserve can be defined as the ability to use different cognitive strategies to optimize performance by calling on alternative neural networks to achieve the task goal. Cognitive reserve is built up throughout life on the basis of our education and the cultural and professional activities we engage in. Judy Pa et al. have reported that the higher the level of cognitive reserve, the lower the effect of exercise. The experience accumulated over a lifetime through physical activity is one way of building cognitive reserve. Learning mathematics, one or more foreign languages, and acquiring knowledge through school and university are other ways of building cognitive reserve [51]. They consider that cognitive reserve is limited, whatever the means used to reach its maximum capacity.

Thus, if an individual’s cognitive reserve is close to its maximum capacity thanks to the knowledge accumulated during his or her school and university career or working life, the physical activities he or she engages in after retirement will have less impact than for an individual whose cognitive reserve is reduced.

Conclusion

Cognitive vitality is essential for the quality of life and survival of older adults. The age-related decline in cognitive performance is now well established. On the whole, maintaining a physically active lifestyle throughout one’s life or the (re) initiation of regular physical activity leads to the maintenance or improvement of cognitive functioning in older adults. It seems, however, that this relationship between physical activity and cognition is not general but specific to certain functions (such as working memory or executive functions).

Factors such as health, basic cognitive level, gender, socio-professional category, and motivation are all variables that can influence both activity and cognition independently. In view of its impact at various levels, we should encourage regular physical activity, particularly among older adults, who are more likely to adopt a sedentary lifestyle. This is all the more true, given that several studies have shown that regular physical activity significantly reduces the risk of premature mortality and can even substantially increase longevity.

References


