Postponing Cognitive Decline

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Key Messages

- Due to demographic change, dementia represents a major health care issue for our society.
- Although the underlying pathogenesis of AD is not fully understood, several observational studies provide strong evidence for an adverse effect of multiple cardiovascular and lifestyle risk factors.
- Prevention programs and strategies targeting the modification of these factors seem a viable and reasonable approach to mitigate and delay cognitive decline and dementia.
- Various factors including a healthy diet, smoking cessation, a physically active lifestyle and cognitive activity have been proposed to exert protective effects on both physical and mental health.
- The "Health Coaching" program developed by the Swiss College of Primary Care Medicine targeting multiple risk factors may in combination with "BrainCoach" represent a promising, long-term effective and low-cost approach to maintain both physical and mental health.

13.1 Introduction

The increase of life expectancy over the last century is paralleled by an elevated number of individuals with dementia, placing an enormous social and economic burden on society and health care systems, in addition to the devastating consequences for patients and their families. According to the World Alzheimer Report

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2015, there is an estimated 47 million people worldwide suffering from dementia [1]. Based on current simulation models, the number of cases is expected to at least double every 20 years, reaching almost 132 million cases until 2050. However, recent reports suggest that the age-specific incidence of dementia might be decreasing in persons with at least high school diploma, possibly due to an improvement in cardiovascular health [2, 3]. Nevertheless and irrespective of how fast the growth of the number of people with dementia will be, the economic impact associated with dementia is huge and increasing. Worldwide, the current total costs have increased by 35% in the last 5 years and were estimated at US$ 818 billion in 2015, representing 1% of the global gross domestic product [1]. These costs include direct medical care costs (i.e., dementia treatment in primary and secondary care), direct social care costs (i.e., community care professionals and residential home setting), and informal care costs (i.e., unpaid care by family and others) [1].

Although several causes of dementia exist, we will focus this review on its most common cause, i.e., Alzheimer's disease (AD). Despite decades of research, the pathological mechanisms underlying this disease remain largely unclear. However, a broad consensus exists that AD has a complex multifactorial etiology and is modulated by various risk factors [4, 5]. A recent estimation calculated by Norton et al. [6] implies that, taking into account the interdependency of these factors, about one-third of AD cases worldwide may be attributable to seven potentially modifiable risk factors: diabetes, midlife hypertension, midlife obesity, depression, physical inactivity, smoking, and low educational attainment (see Fig. 13.1; see also [4]).

While current pharmacological and non-pharmacological treatments may decelerate disease progression, no curative or disease-modifying intervention exists to prevent the pathogenesis of dementia [7, 8]. Thus, there is a pressing need to identify preventive measures and strategies aiming to maintain brain health and delay cognitive decline. Importantly, as neurodegenerative disorders as AD have a long "silent" phase with no or only very subtle symptoms [9], such preventive programs should optimally be implemented at the earliest possible time when cognitive impairments are not yet manifested [10–12]. Figure 13.2 illustrates that preventive strategies require a lifespan perspective. Thus, children and adolescents need to be targeted with regard to education and, starting at midlife, optimal management of potential risk factors is essential [12].

Different modifiable factors to preserve cognitive health have been described. **A healthy diet** (e.g., Mediterranean) rich in antioxidants, vitamins (e.g., vitamin B12, E, and D), and polyunsaturated fatty acids (e.g., omega-3–[13]) may lower the risk of cognitive decline and dementia by reducing for example the risk for cardiovascular diseases. However, although findings from different studies suggest that specific dietary patterns or nutritional components may represent promising interventions in delaying cognitive decline, evidence in this regard is still weak and further investigation on this topic is needed [14, 15]. Additionally, also **physical activity** is known to exert beneficial effects on brain health. Promising results from different observational and intervention studies, as well as systematic reviews, examining the association between physical activity and the risk of cognitive impairment and dementia, yielded promising results with moderate to strong effects of physical activity on

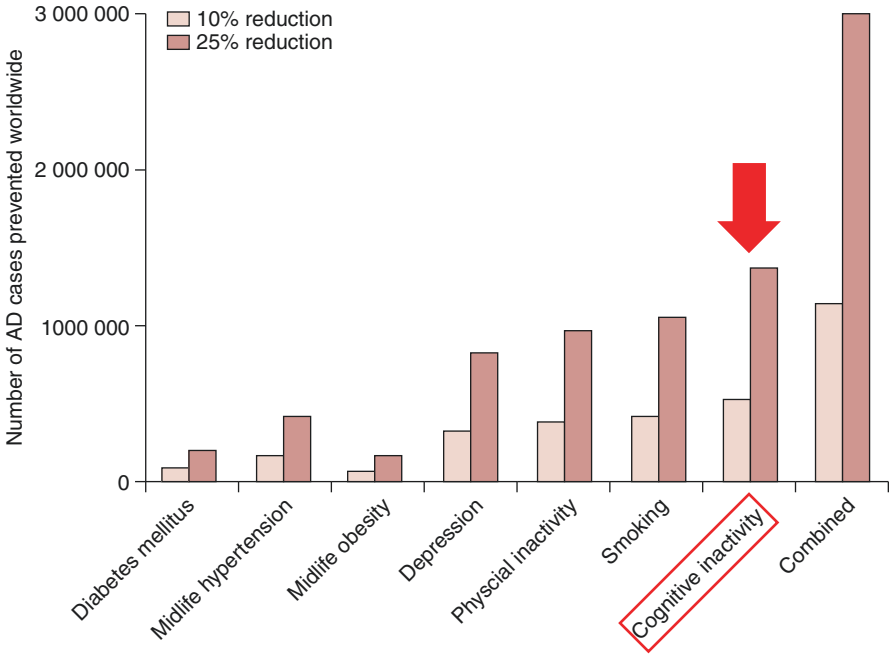

Fig. 13.1 Prevalence and estimates for population-attributable risks (PAR) for Alzheimer's disease (AD) in 2010 (Data source: Norton et al. [6]). PAR = population-attributable risk, i.e., the proportion of AD cases in the population that can be attributed to individual risk factors calculated by using the population prevalence and the relative risk of the risk factor. Combined = calculated prevalence and PAR for the seven individual risk factors combined, assuming independence of the risk factors. Adjusted combined = calculated prevalence and PAR for all seven risk factors combined with adjustment for non-independence of the risk factors

brain health. These results indicate that individuals with a physically active lifestyle exhibit less cognitive decline [16], reduced brain atrophy [17], and increased hippocampal volume [9] compared to people with a sedentary lifestyle. A third important protective factor for the maintenance of brain health is **cognitive activity**. This aspect will be reviewed in more detail below and a "BrainCoach" program, which focuses on cognitive activity as a preventive measure of cognitive decline, is introduced.

13.2 Cognitive Activity as a Modifiable Protective Factor for Cognitive Decline

As shown in Fig. 13.1, low educational attainment [6] or cognitive inactivity [4] constitutes the largest single risk factor for AD. Certainly, a high educational attainment will not prevent pathological brain changes. However, a number of studies indicate that higher educational attainment is related to higher levels of cognitive performance and seems to buffer negative effects and mitigate clinical symptoms in

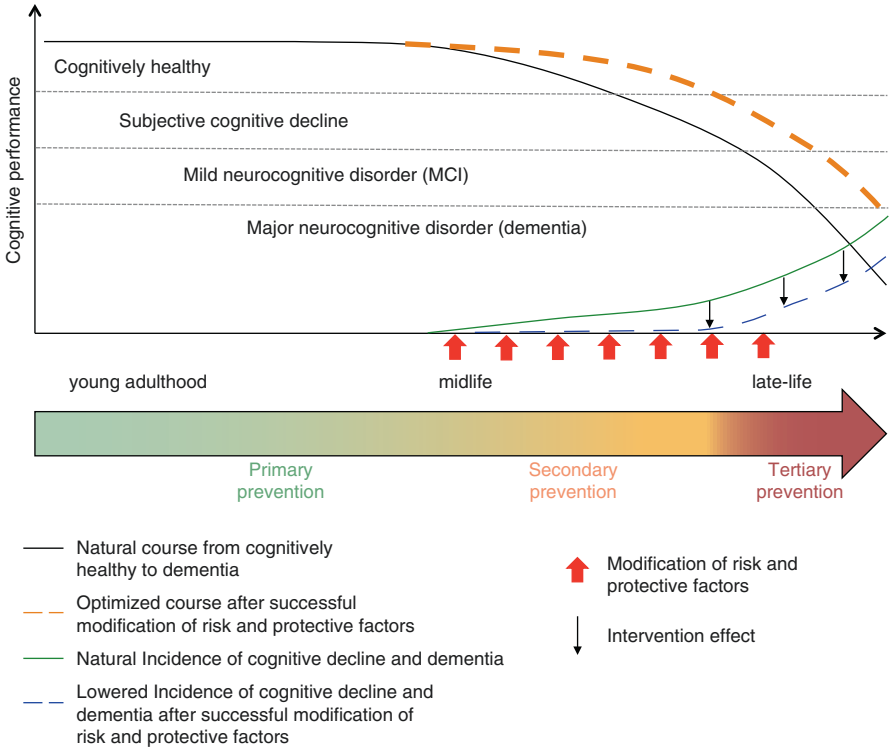

Fig. 13.2 Hypothesized model of neurocognitive disorders [12] across lifespan without (black line) and with (orange dashed line) successful modification of risk and protective factors and the consequence on dementia incidence rates: natural course (green line) vs. result of optimally timed preventive strategies through primary, secondary, and tertiary prevention (blue dashed line) (figure adapted from [36] (reproduced with permission), [18] (reproduced with permission: © 2014 The Association for the Publication of the Journal of Internal Medicine))

everyday life [2, 18, 19]. The rationale behind this observation is the hypothesis that higher educational attainment results in an increased cognitive reserve [18]. This so-called cognitive reserve hypothesis implies that individuals with higher levels of brain activity (e.g., through individual or synergistic contributions of high educational/occupational attainment and maintained cognitive activity up until old age) may better cope with brain pathology and are able to compensate brain damage much longer because of increased synaptic densities and a more complex and efficient structure of neural networks [18]. Thus, people with the same extent of pathological brain changes may exhibit different clinical manifestations of the disease depending on their level of cognitive reserve (see Fig. 13.3 [20]). Importantly, a person with a high cognitive reserve will have a steeper decline once symptoms are manifest due to higher pathological brain accumulations until cognitive dysfunctions are clinically perceivable [20].

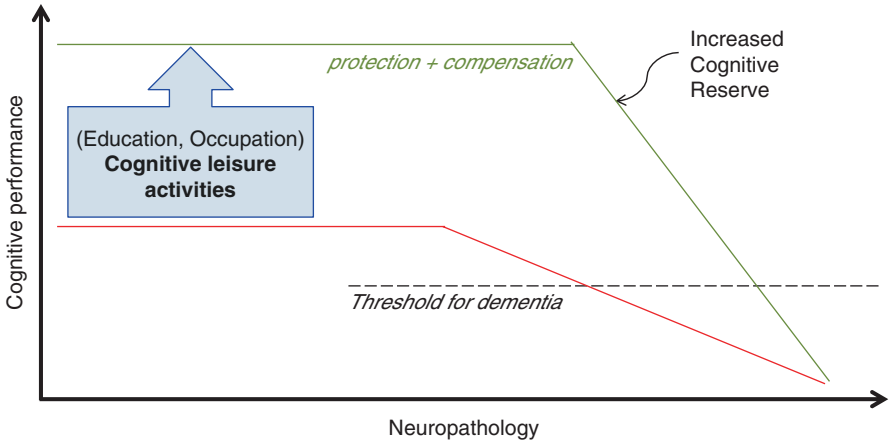

Fig. 13.3 Illustration of the association between the emergence of dementia-associated neuropathology, its clinical expression and cognitive reserve (figure adapted from [21]; reproduced with permission). Educational attainment and occupational challenges can usually no longer be changed in individuals aged 50 years and older. However, cognitive leisure activities may increase their cognitive reserve and thus lead to a delay in the emergence of cognitive decline

These findings are supported by several studies reporting reduced incidence rates of cognitive impairment and dementia in older adults with a high educational attainment [2, 19]. Additionally, an analysis from Barnes and Yaffe [4] indicates that the relative risk (i.e., the ratio of the probability to develop dementia in an at-risk group compared to a non-risk group) for dementia in people with a low education (i.e., with only primary education) is 59% higher compared to people with a higher education.

However, older adults experiencing a cognitive decline obviously already completed their formal and occupational education. The cognitive reserve, though, is not influenced by education alone. Retrospective studies indicate that significant associations exist between cognitively activating leisure activities, engagement in social activities, the level of cognitive performance, and the risk of dementia [21, 22]. Moreover, studies show that performing cognitively stimulating leisure activities later in life may somewhat compensate for a low educational attainment [23, 24]. Thus, cognitive reserve is not a static condition—it can be influenced and enhanced at any point in someone's lifetime.

There is great diversity of cognitive tasks and their duration of exposure in different studies investigating the association between cognitive activity and the risk of dementia. Thus, some studies also brought some inconclusive findings. Nevertheless, there is substantial evidence that participating in cognitive activities conveys beneficial effects for the maintenance of brain health and may delay cognitive decline [22]. Different experimental studies on rodents [25] and imaging studies on humans [26] suggest that a mentally stimulating environment promotes neurotrophic changes in the hippocampal formation, neurogenesis, and synaptic density. An

imaging study by Valenzuela et al. [26] with healthy older human adults shows that participants with high levels of mental activities (in the domains of education, occupation, creative arts, reading, writing, socializing, and day-to-day habits) across the lifespan (young adulthood, middle age, and late life) exhibit a reduced rate of hippocampal atrophy compared to those with low levels.

A Cochrane review [27] examining the effect of cognitive training (i.e., the structured practice on tasks targeting specific domains of cognitive functioning) with 36 included studies involving healthy older participants or people with mild cognitive impairment provides evidence for an improvement in immediate and delayed verbal recall compared to participants without training. However, this positive effect did not exceed the improvements in active control groups receiving "only" unspecific cognitive stimulation such as reading, playing board games, or dancing that may significantly reduce the risk for cognitive decline or dementia (see also e.g., [28]). Moreover, various studies revealed that musical activities (i.e., playing an instrument or singing) enhance performance in different cognitive domains (attention, executive functions) by promoting neural plasticity and increasing gray matter volume in frontal, motor, parietal, and temporal (e.g., hippocampus) areas [29].

In summary, there is hopeful evidence that non-pharmacological interventions in stages with no or very little cognitive impairment may be effective in delaying (further) cognitive decline. Optimally, such a program should address all possible preventive aspects: dietary habits, physical activity, intake of toxic substances (smoking behavior and alcohol consumption), and cognitive activity.

13.3 Prevention Studies with a Multidimensional Approach

Although observational studies confirm the association between the mentioned modifiable risk factors and AD, results from intervention studies investigating the effect of these factors in delaying the onset of cognitive decline or AD are mixed. These inconsistent findings may have resulted from various methodological problems including small samples, short intervention periods with short follow-ups or inappropriate timing (too late to obtain a significant intervention effect; or a mono-interventional approach investigating only one risk factor [10]). However, as the underlying pathology of AD is multifactorial, measures addressing multiple target areas aiming to modify vascular and lifestyle factors simultaneously seem more appropriate. To date, there are three large ongoing European intervention studies targeting simultaneously multiple risk factors: the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (**FINGER**; [30, 31]), the Prevention of Dementia by Intensive Vascular Care (**PreDIVA**, [32]) study, and the study Multidomain Alzheimer Preventive Trial (**MAPT**, [33, 34]). Until now, only preliminary results from these studies have been published. In 2011, the European Dementia Prevention Initiative (**EDPI**; http://www.edpi.org/) was launched to combine the valuable information collected in the three ongoing European trials mentioned above. The aim of this initiative is to improve and promote the

collaboration between researchers involved in the field of dementia prevention to combine experience and datasets and better define target populations, intervention strategies, and methodological challenges in large dementia prevention trials [10]. Based on the studies mentioned above, an innovative and interactive Internet intervention platform for the treatment of cardiovascular disease in older people was initiated as an additional project by the members of the EDPI called Healthy Aging Through Internet Counseling in the Elderly (**HATICE**; http://www.hatice.eu/). An additional initiative from Switzerland named "**EviPrev"** is based on current scientific data and focuses on evidence-based prevention and early detection of potentially chronic diseases (short interventions on physical activity, nutrition, smoking, alcohol consumption and screening for high blood pressure, dyslipidemia, diabetes, breast cancer, colon cancer, and others) in primary health care setting. Although this project is not considered to be a prevention study with a multidimensional approach, it has an important impact on cognitive health by systematically recording cardiovascular risk factors. A systematic assessment of these risk factors which significantly affect cognitive health is crucial for effective treatments and successful lifestyle interventions [35].

13.4 Health Coaching: A Multidimensional Counseling Program to Promote Health Behavior in the Primary Care Setting

Based on the findings summarized so far, an additional multidimensional and structured health program of counseling in primary care practice called "Health Coaching" was developed by the Swiss College of Primary Care Medicine (http://www.gesundheitscoaching-khm.ch/; [36]. Designed for GPs, the primary aim of this program is to promote health behavior in the Swiss population and prevent chronic diseases (e.g., stroke, coronary heart disease, cardiovascular disease) by targeting the most important contributors to disease burden including smoking, alcohol consumption, body weight, dietary habits, level of physical activity, and coping strategies with stress [36, 37]. The aim is to give GPs the tools to motivate their patients and accompany them during the implementation of a healthier lifestyle. Patients are involved in the decision process and share the responsibility for their health with the practitioner. Thus, an important aspect of "Health Coaching" is that patient and health professional meet on equal terms and jointly plan a step-by-step health program based on the patient's individual preferences and abilities [36]. The program also emphasizes the high importance of the GPs' communication skills and offers specific training programs in Motivational Interviewing (MI; see below) within this program [38]. Although Health Coaching as a non-pharmacological program is certainly quite comprehensive and probably sufficient for individuals who are still in work force, it could benefit from an additional module focusing on cognitive activity for patients who are beyond retirement or who exhibit subtle cognitive problems.

13.5 BrainCoach Program to Promote Cognitive Activity

13.5.1 Cognitive Activity

Based on scientific data reviewed above we have developed a cognitive activity program named "BrainCoach," which was specifically created for older adults at risk for cognitive impairment who might be e.g., in the so-called "silent phase" of AD [39] and is meant to be implemented in the primary care setting to be conducted by the GPs and other health care professionals (e.g., psychologists). The primary purpose of this module is—in accordance with the theory of cognitive reserve described above and the rule of "Use it or lose it!"—to accompany older adults and promote their motivation to maintain and increase brain health by increasing their cognitive activity. The program addresses especially older adults feeling cognitively "bored" in everyday life, individuals being shortly before retirement, or individuals with subtle cognitive alterations. The promotion of the activity will be achieved by a specific folder (A4-format) including information about cognitive activity and its effects on brain health, communication skills (Motivational Interviewing), and a structured questionnaire as a guideline (working sheet) to evaluate the patients' current cognitive activity and increase their motivation to find and implement a cognitive activity in their daily life. The "BrainCoach" program intentionally does not include specific cognitive exercises but highlights the importance of eliciting the patients' motivation to find a cognitive activity that they like to perform regularly (e.g., something they performed earlier in their life). In case the patients cannot think of any cognitive activity they would like to engage in, the "BrainCoach" program offers a range of different cognitive activities—a "cognitive buffet" (i.e., different activities depicted on color photographs)—from which the patients may choose the ones they would like to perform. Some possible activities can be performed individually such as doing artwork, solving crossword puzzles, singing, playing a musical instrument, or reading books/newspapers. Activities carried out in groups have an additional stimulating component, especially due to social interactions. Examples for these kinds of activities include language courses, dancing classes, singing in a choir, reading circles, attending university for seniors, playing board games, or attending cultural events with friends (e.g., theater, cinema, and concerts). This list included in the "BrainCoach" program cannot be complete, since a variety of additional activities may positively affect brain health. The patients are free in choosing something from this list or engage in another cognitively stimulating activity. The "BrainCoach" program is cost-free; however, the chosen activities have to be paid by the patients.

13.5.2 Motivational Interviewing (MI)

Mathematically speaking it would make the most sense to especially inspire patients with a low cognitive reserve to (newly) engage in cognitive activities,

since these individuals have the largest room for improvement (see Fig. 13.3). Thus, the technique used to motivate patients will be critical. MI is a well-known client-centered and collaborative counseling technique that has frequently and successfully been applied in general health care settings and health promotion [40]. Briefly, eliciting people's intrinsic motivation appears to be a key factor to achieve long-lasting behavioral change [41–43]. For example, in the "BrainCoach" program a cognitive activity is chosen from the cognitive buffet because of the patient's personal interest in the activity. Its motivation is more likely to be intrinsic, because the patient probably chose this activity for being enjoyable, pleasurable, or giving satisfaction. Importantly, because patient and health practitioner work together at eye level to identify a suitable cognitive activity, engagement in this activity is not extrinsically motivated. That is, the patient does not engage in this activity to receive a reward, or because of feeling obliged. MI can be used in a brief intervention format, making it suitable for the primary care setting. As motivating and accompanying patients to make health-related behavioral changes represent a challenge for GPs, profound communication skills are crucial for successful counseling. Within the "BrainCoach" program, a training program for GPs in MI has been developed.

The "BrainCoach" program, including the folder, the "cognitive buffet," and a structured questionnaire (work sheet) based on the communication skills included in MI has been tested in a pilot study (feasibility, acceptance of the documents and the concept) and resulted in very high acceptance rates in both GPs and patients.

Conclusions

Due to demographic change, dementia represents a major health care issue for our society. Although the underlying pathogenesis of AD is not fully understood, a number of observational studies provide strong evidence for an adverse effect of multiple cardiovascular and lifestyle risk factors. In this regard, prevention strategies are needed to manage and lower the increase of dementia cases influenced by these risk factors. Delaying cognitive decline and dementia would have a huge impact on its incidence and prevalence. Specifically, a 10–20% reduction of the seven main risk factors for AD (diabetes, midlife hypertension, midlife obesity, physical inactivity, depression, smoking, low educational attainment) would decrease AD prevalence by 8–15% until 2050 [7]. Additionally, estimations from a projection model imply that interventions with the potential to delay disease onset or progression by only 1 year would reduce the number of AD patients by about 11% (i.e., nine million cases; [43]). Understanding the contribution and the impact of different lifestyle factors on disease development will have an important influence on future disease management and treatment since many of these risk factors are modifiable.

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