A REVIEW OF MULTIDOMAIN INTERVENTIONS TO SUPPORT HEALTHY COGNITIVE AGEING

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Abstract: Objective: The risk for cognitive decline and for developing Alzheimer’s disease increases with age. The aetiology is assumed to be of multi-factorial origin, and treatment opportunities are lacking. Despite the multi-factorial origin, many intervention studies focused on single factors to influence cognitive health with inconsistent findings. In this view, more and more intervention studies aim to intervene on multiple factors simultaneously to affect or slow down cognitive decline. The purpose of this paper is to give an overview of these multidomain intervention trials. Methods: We conducted a non-systematic literature search in Medline, Scopus, Cochrane Library, and clinical trials databases up to October 2011 to review multidomain interventions that investigated effects of combined lifestyle-related factors on cognitive decline and the progression of dementia. Results: Interest in multidomain interventions increased over the past years. We identified six completed and published trials and eight ongoing or not yet published studies that investigated effects on cognitive outcomes. First completed trials yielded promising results for the combination of exercise and mental training and diet and behavioural weight management. Results of ongoing multidomain trials are awaited. Conclusions: Some evidence suggests that strategies which target multiple factors simultaneously may prove more effective than those focusing on a single mechanism or domain. Larger high-quality randomized controlled trials are required to systematically investigate the cognitive effect of programs comprising physical and mental activity as well as nutritional aspects.

Key words: Healthy ageing, multidomain interventions, mental activity, physical activity, diet.

Over the last few years, the population aged 60 years or over has grown faster than any other age group. This increase poses a series of new challenges to our society, such as a rising demand in various forms of health and welfare care. Therefore, there is an urgent need for development of various strategies to help the elderly remain in good physical and mental health, so that they remain independent and continue to play an integral part in the family and community life. The role played by modifiable environmental factors in the prevention of cognitive decline and neurodegenerative diseases such as Alzheimer’s disease and other types of dementia is not yet well understood. Yet, the cognitive deficits and behavioral abnormalities associated with this condition are the major cause of disability in the elderly (1). The potential benefit of preventive strategies to support healthy ageing is enormous. It is estimated that delaying the onset of dementia such as Alzheimer’s disease by only one year would reduce its prevalence by about 25% (2).

Over the past decade, the notion that cognitive impairment and dementia may result at least in part by a lifelong cumulative effect of different risk and protective factors of genetic, biological and psychosocial origin as well as their interactions has gradually emerged (1, 3, 4). The observation that age is the strongest risk factor for dementia has largely contributed to this view. Indeed, it has been reported that the incidence rate of Alzheimer’s disease increases almost exponentially with increasing age until 85 years of age (3). In the United States, Alzheimer’s disease has been estimated to affect almost 50% of adults over their lifespan (5), which suggests that dementia may be an inevitable consequence of ageing.

Numerous epidemiological findings indicate that various lifestyle-related factors may play an important role in the development of cognitive impairment and dementia in elderly people. However, randomized controlled trials targeting at modifying single factors, such as cardiovascular disease factors (e.g. hypertension, hypercholesterolemia and diabetes mellitus), physical activity, mental activity, as well as diet and nutrition, often resulted in inconsistent findings or insufficient evidence (for review see for instance (6-8)). Most promising effects were reported for antihypertensive therapy (9-11), intranasal insulin (12, 13), long-term physical activity programs (> 6 months) (14-21), certain mental stimulating activities (speed of processing training and reasoning training) (22), and adherence to Mediterranean diet (23, 24).

Inconsistent findings and the difficulty to demonstrate cognitive effects in single intervention trials may be partly due to methodological limitations. Alternatively, single, isolated intervention approaches may be too simplistic with regard to the complex, multi-factorial nature of cognitive impairment. In view of that, recent observational studies suggest that leisure activities containing multiple components (e.g. mental, physical, and social) may be more beneficial than activities containing only one component (25-27). This development towards multidomain approaches to support healthy cognitive ageing or to slow down cognitive decline can also be observed in study designs of recent intervention trials. In this review, we present an overview of trials that modify simultaneously multiple lifestyle-related factors in healthy elderly subjects or
in subjects at risk for cognitive impairment to affect cognitive performance and the risk for developing Alzheimer’s disease.

Methods

We conducted a non-systematic literature search with no specific criteria for quality assessment in Medline, Scopus, Cochrane Library, and Clinical Trials databases up to October 2011 to review interventions that investigated lifestyle-related factors and their effects on cognitive performance. Trials were considered appropriate if they included cognitive outcomes, investigated healthy or cognitively impaired older adults and if non-pharmacological interventions aimed at modifying several lifestyle-related factors simultaneously, such as mental stimulation plus physical activity or physical activity plus a nutritional intervention and so on. Search terms were exclusively used in English and comprised for instance “mental health”, “cognitive decline”, “cognition”, “physical activity”, “cognitive training”, “nutrition”, “diet”, “social engagement” “lifestyle”, “elderly”, and combinations thereof.

The search procedure was not systematic and cannot be considered as comprehensive.

Results

Following our literature search, we identified 6 completed and published, non-pharmacological multidomain intervention studies (table 1) as well as 8 ongoing or not yet published, non-pharmacological multidomain intervention studies (table 2) to investigate cognitive effects in elderly people. Hereafter we present a short description of the trials.

Completed Multidomain Trials

Three of the completed multidomain trials investigated physical exercise and cognitive training either alone or in combination. In the SimA study conducted in Germany, 375 healthy elderly subjects aged 75-93 years were assigned into 6 different groups: psychoeducational training, cognitive training, physical training, psychoeducational and physical training, cognitive and physical training, or control group (28, 29). The psychoeducational training focused on various needs (e.g., technical aids in the household, problem solving in everyday life, etc.). The cognitive training focused on information processing speed, attention and memory functions. The physical training consisted in training of balance, perceptual and motor coordination, and flexibility. The training occurred every week over 9 months, and each session lasted between 45-135 minutes depending on the group assignment. Participants were followed up to 5 years. Various domains of outcomes were measured, such as cognitive function (information processing speed, attention, primary and secondary memory, long-term memory and reasoning), physical function, emotional status, independent living, and health status. The authors reported that participants in the combined cognitive and physical training displayed sustained improvements in most domains as compared to the control group. Among the best improvements were those seen in cognitive functions, cognitive impairment, health status and depression. Interestingly, the cognitive outcome measures in the combined cognitive and physical training group appeared to be better than in the single cognitive training group. Similar findings were reported from a small study in France (30). Thirty-two healthy elderly subjects aged 60-76 years were allocated into four different groups: aerobic training, mental training, combined aerobic and mental training, and a control group. The authors reported that 2 months of combined aerobic and mental training provided greater effects on memory scores than either treatment alone. The third cognition and exercise trial, the Seniors Health and Activity Research Program Pilot (SHARP-P), investigated the effect of a 4-month training program in 73 community-dwelling older people aged 70-85 years and at risk for cognitive decline (31). Participants received cognitive training, physical activity sessions or both. The cognitive training consisted of 2 computer-based sessions per week, 40-45 minutes each, and targeted at improving memory and executive functions. The physical activity sessions aimed on aerobic and flexibility training for 150 minutes per week, including 2 centre-based sessions of 60 minutes each and additional home-based training. Participants of the combined intervention received both trainings on the same day. The control intervention comprised weekly health education lectures. Outcome measures included executive functioning, episodic memory, and physical function. No treatment led to statistically significant differences in 4-month changes in cognitive outcomes. For data interpretation it should be considered that the trial was a pilot trial and designed to obtain information on required sample sizes.

Another three completed trials identified for this review included diet-related interventions; two studies in frail elderly people, one in overweight or obese older people with high blood pressure. In a Dutch study, De Jong et al. (32) randomized elderly people aged 70 years and older and at risk of suboptimal micronutrient status, functional decline, and neurological disorders to a 17-week intervention of enriched foods plus a social program, regular foods plus exercise, enriched foods plus exercise, or regular foods plus a social program. In the nutrition condition of enriched foods participants were asked to consume 2 products daily in addition to their regular diet: one fruit-based product and one dairy product. These products delivered 100% of the Dutch recommended dietary allowance of several vitamins and minerals. The exercise program emphasized on muscle strength, coordination, flexibility and speed and lasted 45 minutes, twice a week. The social program focused on creative and social activities. It served as a control for the exercise program and lasted 90 minutes every other week. Outcome measures included psychomotor speed and biochemical indexes. While enriched foods showed positive effects on