

Received: 2014.09.21
Accepted: 2014.10.31
Published: 2015.02.24

Guidelines for Prevention and Treatment of Cognitive Impairment in the Elderly

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 **Andrzej Brodziak**
BCDF 2 **Agnieszka Wolińska**
BCDF 2 **Estera Kołat**
BCDF 2 **Alicja Różyk-Myrta**

1 Independent Researcher, Institute of Occupational Medicine and Environmental Health, Sosnowiec, Poland
2 Institute of Nursing, University of Applied Sciences, Nysa, Poland

Corresponding Author: Andrzej Brodziak, e-mail: andrzejbrodziak@wp.pl
Source of support: Self financing

The aim of this study is to present the available and verified methods of prevention of cognitive decline in healthy older adults and to review clinical trials of therapies to improve impaired cognitive performance. We discuss data about the actual possibility of pharmacological treatment, usefulness of physical exercises, and effectiveness of different cognitive training methods.

In a separate chapter we discuss why older people cope much better in life challenges than it would appear from the measurements made by use of neuro-psychological tests.





We also discuss the so-called issue of transfers, ie, the question of how certain cognitive characteristics, improved through cognitive training, are transferred to other mental skills.

We distinguish between simple and sophisticated (usually computerized) forms of cognitive training and pay particular attention to methods that are simple and easy to use. In particular, we discuss the so-called "learning therapy", which amounts to "reading aloud and simple arithmetic calculations", the method based on "switching between words and imagination", and also the method consisting of personal counseling, support, and assistance in learning, especially in the form of home visits.

In the final chapter we formulate practical advice, not only for individuals who want to undertake the preventing or correction activities alone with eventual help of medical professionals, but also for the members of health institutions that wish to implement preventive and therapeutic actions directed to a chosen population. We also discuss the indications and rationale for further research and clinical trials.

MeSH Keywords: **Cognitive Therapy • Health Services for the Aged • Mild Cognitive Impairment**

Full-text PDF: <http://www.medscimonit.com/abstract/index/idArt/892542>

 7815  1  —  56



Background

Elongation of the average life span and the decline in the birth-rate leads in many countries around the world to an increased proportion of older people in the population, which is called “the aging of society”. Demographic changes have already forced the authorities of most countries to extend the working time before retirement. At the same time, the expectation of older people to be physically and mentally fit is increasing.

In these circumstances, many researchers wonder whether it is possible to prevent the decline of cognitive performance of older people [1]. Other researchers are trying to assess whether the decline in cognitive performance of elderly people impairs the actual ability to cope with the challenges of everyday life and the fulfillment of professional tasks [2–5].

Many teams of researchers recently carried out long-term controlled clinical trials of various methods which could potentially improve the cognitive functions in the elderly [6–11].

There must be, however, a distinction between natural decline of mental capacity in elderly and the occurrence of so-called “mild cognitive impairment” [12–15]. Some of these studies have just focused on attempts to decrease consequences of premature mild cognitive impairment [16–19].

The discussed issues are very important because many authors and institutions promote a whole range of different methods. Use of some of these methods may be very cumbersome and can be hard to maintain in older people. Decisions to attempt to prevent the deterioration of cognitive performance in the elderly or attempt to improve the mental efficiency cause a difficult dilemma for health professionals about which methods of cognitive interventions should be used.

According to some authors and our own experience, the long-term cognitive training based on performing complex (usually computerized) puzzles and other similar mental tasks is often discontinued. These actions are abandoned, although their impact is possible only when they are constantly used. However, there are many common, natural, demanding intellectual tasks that are performed by some people with willingness and interest. One can enumerate as examples of such activities: reading novels, writing memoirs or autobiography, learning a foreign language, playing board games, and traveling. This raises the question of whether such intellectual activities, as a form of cognitive training, were already proposed and tested.

So, we decided to review and discuss in this paper the most important controversy regarding the methods of improvement of cognitive performance and provide data about the real effectiveness of different strategies of prevention and treatment.

We pay particular attention to methods that are simple and easy to use and even to rules of personal guidance, assistance, and help in teaching, especially in the form of home visits.

Understanding the essence of sophisticated methods of assessment and cognitive training, as well as comparison with simple methods, may present difficulties for those readers who are not familiar with computerized methods. It seems to us, however, that readers not familiar with such methodology of cognitive training can now easily become familiar with the substance of such interventions by reviewing the tools easy accessible in the Internet. We gathered in Table 1, attached to this paper, of examples of basic elements of this kind of training, such as measuring the time of reaction, efficiency of reflex, capacity of short-term memory, ability to divided and selective attention, and perceptivity. The Table 1 also provides URLs to examples of computerized systems realizing the cognitive training (partly free access) and open websites that contain sets of games helpful for the realization of cognitive training (partly free access). It should be noted at the outset that examples of such methods listed in the table appearing in the Table 1 are not standardized tools and one should consider them only as an illustration of the presentation.

Frequency of Cognitive Impairment in the Elderly

Over the years, the capacity of many cognitive processes deteriorates, which can be determined by neuro-psychological measurements. It is in fact a normal, physiological process [1] and must be discerned from some pathological syndromes.

Cognitive decline in older people often manifests as so-called “mild cognitive impairment” (MCI), which means that cognitive capacity is below that normally expected in a person of the same age [13,14]. Naqvi et al. conclude in their review paper that mild cognitive impairment affects 10–25% of people over the age of 70 years. The annual rate of conversion from mild cognitive impairment to dementia is about 10% [1,19,20]. Dementia is defined as cognitive decline in 1 of several cognitive domains, along with difficulty in functional abilities.

Lin et al. reviewed 1190 articles related to the screening for cognitive impairment in older adults [15]. These investigators concentrated on tests used to detect dementia. They found that The Mini-Mental State Examination was used most frequently. They conclude that “...brief instruments to screen for cognitive impairment can adequately detect dementia, but there is no empirical evidence that screening improves decision making”.

Marshall et al. proposed recently the “everyday cognition scale”, which discriminates effectively between people who

Table 1. The table contains URLs of websites related to some simple tools for elementary psychophysical testing and to several websites providing complex systems for performing cognitive training. These data can facilitate understanding the content of this article, but they serve only as demonstrations. They are not standardized tools suitable for use in research.

	Measured parameter or a particular tool	URL of the website presenting the particular software tool
1	Time of reaction	http://www.brainmetrix.com/brain-reflection/
2	Measuring of the efficiency of reflex	http://www.brainmetrix.com/reflex-test/
3	Simple test of short term memory	http://www.brainmetrix.com/memory-test/
4	Test for ability to divided attention	http://www.militantplatypus.com/games/gamepage.php?game=divided+attention#
5	Test for selective attention	http://www.mindmagician.org/vidsimons1.aspx
6	Test for perceptivity	http://www.mindgames.com/mindgame.php?mind=Rlax&game=131
7	The online Stroop effect tests	http://www.onlinestrooptest.com/stroop_effect_test.php https://faculty.washington.edu/chudler/words.html
8	Test of efficiency of logical thinking	http://brainpages.org/seesaw-logic/
9	An example of a computerizing comprehensive system realizing the cognitive training (partly free access)	http://www.lumosity.com/
10	An example of a free, open website that contains sets of games helpful for the realization of cognitive training (partly free access)	http://www.mindgames.com/
11	Basic information about so called „brain games” on example of “Big Brain Academy” tested by authors of cited paper [40]	http://www.bigbrainacademy.com/
12	The free access website of so called “Brain Age” discussed in the cited paper [29]	http://www.freebrainagegames.com/
13	Basic information about so called “Tetris game”, which is compared to above mentioned “Brain Age” by Nouchi et al. [40]	http://www.tetrisfriends.com/
14	The website.: ” Cogtest – The definitive solution for cognitive testing. Tower of London”, which enable to comprehend the Tower of London task proposed as cognitive training by Rainville et al. [41]	http://cogtest.com/tests/bacs_nonint/tlflash1.html
15	Advices for people counteracting the symptoms of dementia	http://www.alz.org/we_can_help_brain_health_maintain_your_brain.asp

are clinically normal and people with mild cognitive impairment [21]. Early detection of MIC may also be aided by the findings of recent studies on early occurrence of disturbances of orientation in space [22,23]. It seems, however, that the formulation of precise diagnostic criteria for occurrence of MCI is still a challenge.

The Currently Used Method of Prevention of Cognitive Decline in Older Healthy Adults

Naqvi et al., in their initial search of databases found 5205 articles related to the prevention of cognitive decline in older healthy adults [1]. After applying the criteria developed by the Cochrane Effective Practice and Organization of Care Group,

these researchers included only 32 articles in the final analysis. As the result of their analysis, the authors formulated some interesting conclusions related to contemporary possibilities of preventive and therapeutic actions.

Possible pharmacological interventions

Over the past 20 years, many attempts have been made to prevent or correct the mental capacity of people with such groups of drugs as: 1. Cholinesterase inhibitors and N-methyl-d-aspartate glutamate receptor antagonists (donepezil), 2. Hormonal therapies (Estrogen, Testosterone, Dehydroepiandrosterone), 3. Miscellaneous substances like Ginkgo biloba, Vitamins (vitamin B6, E, omega3 fatty acid), candesartan, naproxen, rofecoxib, celecoxib, and rivastigmine.

Naqvi et al. conclude “There is no consistent evidence of benefit for any pharmacologic agent in preventing cognitive decline in healthy older adults”. Studies investigating estrogen therapies and anti-inflammatory medications have shown even a decline in memory capacity.

In our view, it would be advisable to perform studies on the efficacy of long-term use of medications improving the blood supply to the brain, like Vinpocetinum. We should note also recent promising animal studies regarding the pending new pharmacological substances [24,25,27].

Physical exercises

Naqvi et al. found 3 reliable randomized control trials investigating the impact of physical exercise in preventing cognitive decline. Cassilhas et al. investigated resistance-training exercises compared with a placebo stretching group in a study involving 62 men, observed through 6 months [28]. The authors found a statistically significant improvement in some, but not all, tests of short-term and long-term episodic memory.

Brown et al. designed a randomized controlled trial aiming to determine the effect of a general group-based exercise program on cognitive performance and mood among seniors without dementia living in retirement villages [29]. Participants were randomized to 1 of 3 experimental groups: (1) a general group-based exercise (GE) program composed of resistance training and balance training exercises; (2) a flexibility exercise and relaxation technique (FR) program; or (3) no-exercise control (NEC). The GE and FR group participated in 1-hour exercise classes twice a week for a total period of 6 months. The authors assessed cognitive performance in the beginning and at 6 months later in 3 domains: (1) fluid intelligence; (2) visual, verbal, and working memory; and (3) executive functioning. They assessed also mood using the Geriatric Depression Scale and the Positive and Negative Affect Schedule (PANAS). The authors found that the GE program significantly improved cognitive performance of fluid intelligence compared with FR or NEC. They concluded that the GE program significantly improved cognitive performance of fluid intelligence in seniors residing in retirement villages compared with our FR program and the NEC group.

Smith et al. conducted a meta-analysis of 29 studies to investigate the possible impact of aerobic exercises on cognitive functions [30]. They concluded that aerobic exercise training is associated with modest improvements in attention and processing speed, executive function, and memory, although there was less effect on working memory.

In recent randomized controlled trials, Nouchi et al. found that 4 weeks of combination exercise and cognitive training

improved executive functions, episodic memory, and processing speed in healthy elderly people [31,32]. Nevertheless, Naqvi et al., in conclusions from their review, present the opinion that “The evidence for physical activity in preventing cognitive decline is weak” [1].

Cognitive training – mental exercises.

Naqvi et al. draw attention to 3 randomized controlled trials (RCTs) investigating the role of various forms of cognitive training, referred by them also as mental exercise [1]. They mention the first publications of the ACTIVE group, and emphasize that Willis et al. investigated the role of cognitive training in reasoning, speed, and memory in 2832 healthy older adults [6]. They draw also attention to investigations of Smith et al., who compared a computerized cognitive training program based on brain plasticity with a general cognitive stimulation program over 8 weeks in 487 older adults [10]. They cite the results of Berry et al., who assessed the impact of 10 hours of computerized visual demonstration training compared with no training in a study of 32 people over 4 weeks. Berry et al. found statistically significant improvement in performance after 4 weeks in the intervention group compared with the control group [11]. Naqvi et al., in their critical analysis of the various possible methods of influencing cognitive abilities, conclude that “Formal cognitive training exercises may have a benefit in preventing cognitive decline” [1].

Apart from these earlier studies discussed by Naqvi et al., one should pay attention to recent publications of results of the large project known as the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) [7,8].

Rebok et al. recently published the final results of 10-year follow-up of a randomized, controlled single-blind trial, performed on a volunteer sample of 2832 persons with mean baseline age of 73.6 years. The objective of the study was to determine the effects of cognitive training on cognitive abilities and everyday function over 10 years of interventions [8]. The authors assumed that cognitive decline is prevalent in older adults and is associated with decline in performance of instrumental activities of daily living (IADL). They maintain that their project, ACTIVE, is the first large-scale, randomized trial to show that cognitive training improves cognitive function and that there is a transfer of acquainted cognitive abilities to daily functions. The authors argue that the effects of cognitive training last about 10 years.

The methodology used by authors consisted of random assignment to 1 of 3 intervention groups (memory, reasoning, or speed-of-processing training) or a no-contact control group. Outcome assessments were conducted after 1, 2, 3, 5, and 10 years of observations.

The utilized interventions were designed for the specific cognitive abilities like memory, reasoning, and speed of processing. Memory training involved teaching mnemonic strategies (organization, visualization, and association) for remembering verbal material. Reasoning training involved teaching strategies for finding the pattern in a letter or word series. Speed of processing training involved visual search and divided attention through identification of an object on a computer screen at increasingly brief exposures.

The importance of training for speed of processing is discussed thoroughly in a separate paper by other members of the ACTIVE team (Wolinski et al.) [9].

The evaluation of outcome performed by researchers of the ACTIVE Group team consisted of: measures of episodic verbal memory using Rey Auditory-Verbal Learning Test (AVLT), the Hopkins Verbal Learning Test (HVLT), and the Rivermead Behavioral Paragraph Recall Test. Reasoning outcomes were evaluated on the basis of measures requiring identification of patterns, including correctness for Letter Series, Letter Sets, and Word Series. Speed-of-processing outcomes consisted on 3 Useful Field of View (UFOV) tasks requiring identification and localization of information. Functional outcomes consisted of evaluation of whether training-related cognitive changes improved everyday function. This was done by the self-reported Minimum Dataset – Home Care (MDS-HC), which assesses performance in the past 7 days related to: meal preparation, housework, finances, health care, telephone, shopping, travel, and need for assistance in dressing, personal hygiene, and bathing.

The tools for evaluation of daily function also included Everyday Problem Solving, comprising the Everyday Problems Test (EPT) and Observed Tasks of Daily Living (OTDL), and Everyday Speed, comprising Complex Reaction Time (CRT).

The authors conclude that the results of their study demonstrate that cognitive training has beneficial effects on cognitive abilities and on self-reported IADL function. Such interventions hold the potential to delay onset of functional decline and possibly dementia. The authors believe that it has great significance for the public health domain.

Another justification of the use of cognitive training methods comes from findings of Sylvie Belleville and Louis Bherer [33]. They emphasize in their review paper that there is a growing body of literature related to brain imaging investigations aiming to assess the effects of cognitive training in healthy aging populations and in persons with early Alzheimer's disease or mild cognitive impairment. At the structural level, cognitive training in healthy aging individuals has been associated with increased brain volume, cortical thickness, and density and coherence of white matter tracts. At the functional level,

task-related brain activation (using fMRI and PET) and fluoro-deoxyglucose positron emission tomography (FDG-PET) were found to be sensitive to the effects of training. Cognitive training increased brain metabolism and task-related brain activation among persons with MCI [33].

Characteristics of Mild Cognitive Impairment and to Date Attempts of Therapeutic Interventions

Burton et al. report that a set of criteria for diagnosing mild cognitive impairment (MCI) was recently proposed by a multidisciplinary group of experts [12]. One of the proposed criteria included preserved basic activities of daily living and minimal impairment in complex instrumental activities of daily living (IADL). This team tried to investigate whether older adults with MCI classified according to these criteria differed from cognitively intact older adults on a variety of measures of IADL. They concluded that individuals with MCI demonstrated poorer IADL functioning compared to cognitively intact older adults. However, the changes in IADL functioning observed in MCI may be too subtle to be detected by certain measures, such as the Lawton and Brody IADL Scale.

Wadley et al. compared 50 patients with MCI and 59 cognitively normal participants [13]. They focused on the comparison of speed and accuracy in performing IADL, using a standardized Timed IADL measure that evaluates 5 functional domains commonly encountered in everyday: telephone use, locating nutrition information on food labels, financial abilities, grocery shopping, and medication management. The obtained results suggest that slower speed of task performance is an important component and perhaps an early marker of functional change in MCI that would not be detected using traditional measurements of daily function. The authors maintain that their finding may improve the prediction of future cognitive decline and disease progression among those individuals in whom MCI foreshadows development of dementia.

Schmitter-Edgecombe et al. evaluated different elements of memory processes and explored their contributions to everyday functional limitations in persons with MCI [14]. They included individuals with amnesic MCI, nonamnesic MCI, and healthy older adults. The amnesic MCI group of patients experienced greater difficulty than controls in completing IADLs.

The same team of researchers, who conducted a 10-year controlled trial of the impact of cognitive training on cognition and everyday functioning in older adults, also published the results of the analysis of changes in the daily functioning of people with MCI [16]. They examined the trajectories of change in everyday function for individuals with cognitive deficits suggestive for mild

cognitive impairment [16]. They examined changes in self-reported activities of daily living (IADLs) on the basis of the Minimum Data Set Home Care Interview in 2358 participants over a 3-year period. All MCI groups showed faster rates of decline in everyday function than cognitively normal participants with no MCI.

Wadley et al. conclude that their results demonstrate that mild cognitive impairment is a separate clinical entity that not only predicts progression to dementia, but also predicts functional declines in activities essential for to autonomy and quality of life [16].

Several teams of researchers published results of trials of applications of different kinds of cognitive training and interventions aiming to improve performance in patients with mild cognitive impairment [17–19].

Huijie Li et al. recently published results of their exhaustive meta-analysis of the effects of cognitive interventions in people with mild cognitive impairment [19]. They emphasize in the introduction to this meta-analysis that persons with MCI are at high risk for progression to Alzheimer's disease (AD) or other types of dementia, with an annual conversion rate of approximately 10–15%, compared with healthy controls whose conversion rate is about 1–2%. [19]. Follow-up studies demonstrate that 80% of MCI converts to AD in about 6 years. They write “MCI has become a hot topic and researchers primarily focus on two issues, one is to look for biomarkers of progression to AD, the other one is to find effective treatment”.

Many researchers found impairment of associative learning and selective loss of person-specific knowledge like naming famous people and object tasks [19]. Persons with MCI also show deficits in episodic and semantic memory. The application of tests that assess simple, divided, and selective attention reveal that persons with MCI show more deficits in divided attention, and less deficits in simple attention. Compared with healthy controls, higher percentages of MCI persons and AD patients have impairments in visual motion processing accompanied by memory deficits, suggesting that visual-spatial impairment may also be a sign of MCI. This was also emphasized recently by Vlček and Laczó [22], which correspond to essential discoveries by Edvard Moser and May-Britt Moser – this year's Nobel Prize winners [23].

Li et al. discussed several studies finding that persons with MCI demonstrate deficits in many aspects of executive functions, including response inhibition, switching, and cognitive flexibility. Persons with MCI also exhibit deficits in quality of life (QoL) and activities of daily living (ADL).

Li et al., similar to the above-quoted Naqvi's team, present the opinion that “up to now there is no effective pharmacological treatment for persons with MCI, especially for the long-term beneficial effect” [19]. These authors state also that “since

persons with MCI cannot benefit much from pharmacological intervention, non-pharmacological cognitive interventions begin to attract a lot of attention”. They analyzed 20 papers related to this kind of intervention, with particular attention to the works of Belleville [17] and Fuacounau [18].

Li et al., performing a meta-analysis of a large number of works whose authors have used very different neuro-psychological tests, decided to distinguish 6 domains of the outcome measures. The first was the episodic and semantic memory tests. The second domain was the executive memory, measured usually by the Trail Making Test – Part B, the Wisconsin Card Sorting Test (WCST), clock drawing, and digit span tests. The third domain focused on attention and processing speed. The fourth domain was visual-spatial ability, including pattern and picture reproduction, and facial recognition test. The fifth was about the changes of the Mini-Mental State Examination (MMSE) during the cognitive intervention. The sixth was emotional state, mainly focusing on depression and anxiety. The authors also compiled data related to activities of daily living (ADL) and QoL.

Li et al. concluded that results of many studies demonstrate that patients with MCI significantly improve after training, both in overall cognition and overall self-ratings. They gain moderate benefits in language, self-rated anxiety, and functional ability, and receive moderate benefits in episodic memory, semantic memory, executive functioning and working memory, and visual-spatial ability, as well as in attention processing speed, MMSE, self-rated memory problem, quality of life, activities of daily life, and self-rated depression. The results also suggest that persons with MCI benefit from cognitive intervention in follow-up. Li et al. emphasized that cognitive intervention may be an efficient method to enhance cognitive and functional abilities in persons with MCI.

Older Adults Cope Much better than it Would Appear from the Measurements Made by Neuro-Psychological Tests

Considerations of justifications of the utilization of different methods of cognitive training and interventions should take into account the important remarks of several authors, who analyzed the real cognitive capacity of older people with the results obtained by them in neuropsychological tests.

Timothy Salthouse noted that a divergence is observed between abilities of older adults estimated on the basis of their behavior in daily life and their competencies estimated by results of neuropsychological tests [2]. According to their performance in neuropsychological tests, older people seem to be considerably less efficient than young adults; however, even persons in their 60s and 70s tend to be highly competent and

have remarkable accomplishments. It is therefore important to clarify why this significant discrepancy exists.

Timothy Salthouse distinguished 2 kinds on neuropsychological tests. One set of tests is designed to assess efficiency in reasoning and memory in a particular moment. The other set of tests is suitable to assess the cumulative results of acquired experience, usually in the form of knowledge, gathered information, and vocabulary. The first kind of test measures the ability to solve novel problems, which could be called “fluid abilities”. The second kind of test measures the so-called “crystallized ability”. Fluid and crystallized abilities vary throughout life. Over the years, there is a monotonic decrease in reasoning ability, but different characteristics of acquired knowledge are stable and decline only in very old age.

Although over the years there may be a decline in productivity, older adults usually have a nearly equal chance of success. Within 20–75 years of age, the indices of overall level of functioning in society are similar.

These observations are confirmed by the meta-analysis of results obtained by many authors studying general mental ability performed by Salgado et al. [3]. Similar remarks were presented by Judge et al. [4].

Effective coping in everyday life and professional achievements of older people can be explained by several overlapping circumstances. Older people seldom need to perform at maximum and frequently rely on accumulated knowledge.

The requirements in everyday life probably correspond to typical load of necessary functioning, whereas the neuropsychological tests tend to estimate our maximal possibilities of functioning. Solving new problems becomes less important because over the years we rely on previously mastered ways to solve encountered tasks.

It also seems that cognition is not the only determinant of success in life. Efficiency at work is probably not only affected by concrete technical skills, but also by “soft skills” like flexible personality traits, attitudes, and effort.

Flexible adaptation to circumstances has a significant role in the elderly. Cognitive capacity can be impaired but this is not noticeable due to adaptation. The accommodation for example, may include the attempts of a person to restrict their exposure to difficult tasks. For instance, many older adults avoid driving in difficult conditions. The adaptation can consist of greater reliance on others and delegation of responsibility to coworkers.

The presence of so many determinants of effective coping in life should be taken in account in shaping of methods of

prevention and improvement of cognitive abilities. Kremen et al. emphasize the significance of real social relations and the stress actually experienced and accumulated in the past [5].

Specific Abilities Improved by Cognitive Training Often do not Transfer to Other Characteristics of Mental Capacity

The researchers realized in the course of the development of various methods of cognitive training that there is a problematic question – “Will the acquired improvements in the domain of certain abilities enhance the performance in other similar cognitive processes?” This is called the problem of transfers of obtained effects and there are many publications related to this topic.

Thompson et al. performed a broad assessment of cognitive abilities and personality traits of young adults who underwent 20 sessions in a working memory training program comparing their post-training performance with a control group [34]. Pre- and post-training measurements of fluid intelligence, standardized intelligence tests, speed of processing, reading skills, and other tests of working memory were assessed. The experimental group exhibited substantial and specific improvements on the trained tasks, which persisted for at least 6 months, but no transfer of improvement was observed to any of the non-trained measurements. The authors concluded that their findings fail to support the idea that adaptive working memory training in healthy young adults enhances working memory capacity in non-trained tasks, fluid intelligence, or other measures of cognitive abilities [34].

Ackerman et al. maintain that to date there are many claims made, but relatively few randomized controlled studies have been conducted to assess transfer of results of cognitive training to another mental capabilities [35]. Therefore, they investigated the effects of 2 specific cognitive training procedures that could influence age-related cognitive decline. A sample of 78 adults between the ages of 50 and 71 completed 20 one-hour training sessions with the Wii Big Brain Academy software (see Table 1) during the first month, and in a second month they completed 20 one-hour reading sessions with articles on 4 different current topics.

An extensive battery of cognitive and perceptual speed ability tests was administered before and after each month of cognitive training activities, along with a battery of domain-knowledge tests. Results indicated substantial improvements in the Wii tasks, somewhat less improvement on the domain-knowledge tests, and practice-related improvements on 6 of the 10 ability tests. However, there was no significant transfer of results of training from the Wii practice or the reading tasks to measures of cognitive and perceptual speed abilities.

According to the authors, the results indicate that the benefits of “using it” in short-term time periods may be limited to the specific tasks which the individual is engaged in, rather than to overall intellectual abilities or other non-practiced tasks. Among the concluding remarks, Ackerman et al. wrote “The findings obtained with respect to transfer effects are not as positive as the developers of ‘brain exercise’ software programs might prefer”. They also note that, to date, the most supportive results for transfer in adult samples have been found for low-structure interventions, long-term interventions, or low-level training such as visual skills [35].

The cited pessimistic opinions of Thompson et al. and Ackerman et al. about the real possibilities for transfer of the acquired skills to other areas of cognitive functions requires consideration of the data on observations made by investigators, who used rather simple forms of cognitive training. We consider such data in the next chapter.

Simple and Sophisticated Forms of Cognitive Training and Interventions

Learning therapy – reading aloud and solving simple arithmetic calculations

Nouchi et al., from the Institute of Development, Aging, and Cancer of Tokyo University, designed a randomized controlled trial with a specific protocol of interventions, which takes into account the results from functional brain imaging in people with cognitive impairments [36]. The authors stated in the introduction to their paper that they developed a new mode of cognitive training using “reading aloud and solving of simple arithmetic calculations”, namely “learning therapy”. They refer to earlier findings of Kawashima [37]. Both reading aloud and solving arithmetic problems require activity of the working memory. The training tasks are extremely simple and easy for elderly people. Consequently, elderly people can readily comprehend and perform the training tasks.

They emphasize that most previous studies involved use of computers, which many elderly people have difficulty using. The difficulty using computers might cause frustration and other negative emotions, possibly reducing their motivation to continue. Nouchi’s training tasks are more familiar to elderly people and thus it was expected to encourage their willingness.

The authors maintain that their procedure is designed for stimulation of frontal, dorsolateral, prefrontal cortex and the temporal and parietal association cortices. The authors targeted these regions because: (1) Recent functional MRI studies showed that task-related activation of these regions in older adults is lower than in younger adults; (2) Previous structural

imaging studies showed that gray and white matter of these regions decline in volume with age; and (3) Activity of these regions is closely linked to cognitive functions such as executive functions, processing speed, and memory, which decrease with age.

The authors investigated the impact of learning therapy on various cognitive functions like executive functions, episodic memory, short-term memory, working memory, attention, reading ability, and processing speed in healthy older adults.

They used a single-blinded intervention in 64 healthy older adults divided into 2 groups: a learning therapy group and a waiting list control group. In the learning therapy group, participants were required to perform 2 cognitive tasks for 6 months: reading Japanese aloud and solving simple calculations. The waiting list group did not participate in the intervention. The primary outcome measure was the Stroop test score, known as a measure of executive function (Table 1). Secondary outcome measures were assessments of verbal fluency task, logical memory, first and second names, digit span forward, digit span backward, Japanese reading test, digit cancellation task, digit symbol coding, and symbol search. The authors assessed these outcome measures before and after the intervention. They maintained that their study provided evidence of learning therapy effectiveness [36] and argued that the protocol of the interventions might engender the positive transfer effect on other cognitive functions [36].

Verbal-to-visual switching.

Osaka et al. are another team of researchers who proposed a specific method for conducting the cognitive training and applied a simple intervention procedure [38]. They investigated a group of 63 people aged 63 years and older. The group was divided into a training group and a control group. They designed the study in such a way that in the first part of the training, participants read aloud 1 sentence and then drew a figure representing the target word on a piece of paper within 60 seconds. In the second part of the training, participants were asked to form a mental image of a figure representing the target word, instead of drawing the image on paper. Both parts of the practice training consisted of 20 trials composed of 3 sentences each and took approximately 1 hour. The participants in the control group read the same sentences and remembered the target words without being instructed to draw or imagine any figures. Using this method, they investigated the effects of verbal-to-visual code switching, which they believe to be the training of working memory performance. Working memory recognition accuracy was enhanced only in the training group.

The authors tried to explore the neural substrates underlying the effects of this training program. They used fMRI to

measure brain activity in both groups during working memory task performance before and after an attention training period. This investigation showed increased activation in the anterior cingulate cortex and in the left and right inferior parietal lobules and right superior parietal lobule [38]. These findings suggest that use of a verbal-to-visual code switching strategy may assist older individuals in the maintenance of information in working memory.

Processing of conflicting tasks

Osaka et al., in another paper, presented their endeavors on verification of the procedures of cognitive training using the tasks that force the divided attention and simultaneous performing of conflicting processes [39]. The authors remark that the working memory of a person is able to perform activities that require dual task performance. Such activities involve attending to goal-relevant information while inhibiting irrelevant information. Impairment of executive function reduces attentional control and contributes to decreased ability to efficiently perform dual tasks [39]. The difficulties arise in performing dual tasks that require inhibitory control of attention, particularly for elderly individuals.

The procedure was aimed at improving attention switching and inhibitory control using the Stroop interference conflict task (Table 1). Words representing color names (e.g., red, blue, yellow) are presented in inks with colors that conflicted with word names. Participants, who were required to name the ink color, had to inhibit the word meaning. Therefore, in naming the ink color, the participants experience strong interference between the word meaning and the ink color. To explore neural substrates underlying performance of conflict activities, 2 working memory tasks were used: a focus reading span test (F-RST) and a non-focus reading span test (NF-RST). The NF-RST test demands greater switching attention due to a conflict between the relevant and an irrelevant task stimulus. Following the Stroop task, fMRI data showed that participants who had engaged in this practice had significant increases in activation in the anterior cingulate cortex, the left inferior parietal lobule, the left dorsolateral prefrontal cortex, and the precuneus region, but a control group, which did not practice, showed no significant increases in these regions. Results suggest that practicing conflict tasks in elderly individuals activates regions related to conflict perceiving and attention switching.

Brain training games and computer-based personalized cognitive training as methods of cognitive interventions

Some researchers have discussed the usefulness of the so-called “brain training games” as a method of intervention aiming to improve the cognitive performance of older people. The use of such games is easy. The team of Nouchi et al. tried to

check the usefulness of these methods [40]. They investigated the impact of the brain training games called “Brain Age” and “Tetris”. Thirty-two elderly volunteers were recruited and randomly assigned to 2 game groups (Brain Age or less demanding Tetris – see Table 1). The participants in both the Brain Age and the Tetris groups played their game for about 15 minutes per day, at least 5 days per week, for 4 weeks. Each group played for a total of about 20 days. Measures of the cognitive functions were conducted before and after training. Measures of the cognitive functions fell into 4 categories: global cognitive status, executive functions, attention, and processing speed. Results showed that the effects of the brain training game were transferred to executive functions and to processing speed. However, the brain training game showed no transfer effect on attention or any global cognitive status. The authors maintain that playing “Brain Age” for 4 weeks could lead to improved cognitive functions, ie, executive functions and processing speed in the elderly. This result indicated that it is possible to improve executive functions and processing speed in short-term training among older people, but long-term effects and relevance for every-day functioning remain uncertain.

Rainville et al. proposed using the Tower of London task to evaluate executive function deficits in persons with mild cognitive impairment [41].

Peretz et al. compared the computer-based, personalized cognitive training versus classical computer games in a randomized double-blind prospective trial [42]. Cognitive performance was assessed in the beginning of the trial and after 3 months by a neuropsychological assessment battery. They found that personalized cognitive training appears to be more effective than computer games in healthy older adults, especially in improving visuospatial working memory, visuospatial learning, and focused attention [42].

Some testing and training methods that are rather difficult to explain in writing are best demonstrated in open-access software tools available on the Internet. For instance, the reader can experience the Stroop test and the Tower of London task by using the software indicated in the attached Table 1.

Personal guidance, assistance, and help in teaching, especially in form of home visits, as a method of cognitive interventions improving mental capacity

Structured procedures consisting of elements such as guidance, assistance, help in writing, and teaching calculation are among the uncomplicated, easy-to-use methods that improve mental and physical capacity of older people. Ukawa et al. recently published results of a randomized controlled trial the “Functioning Improvement Tool Home-Visit Program (FIT-HVP)”,

aiming to impact the cognitive function in older persons [43]. The same team of researchers also compared the effects of applications of the complete FIT-HVP with conversation alone [44].

Their randomized controlled trial included 252 participants aged 65 years or older living at home. Intervention group subjects received a 60-minute FIT-HVP for 3 months. For verification of effects, the authors used the Mini-Mental State Examination (MMSE). They concluded that the FIT-HVP procedure improved cognitive function, but that further studies with larger samples and longer follow-up periods are needed to assess the long-term effectiveness of the method.

Karatay and Akkus presented a similar, but less structured, procedure of home visits to improve cognitive function [45]. They tested the effects of a multipartite home-based intervention program on cognitive function, anxiety, and depression among older adults with cognitive impairment. Their program provides 7 home visits for each senior, including conversations, newspaper or book reading, painting or handcraft activities, and physical exercises. As the verification tools, they used the MSE, the Beck Anxiety Scale, and the Geriatric Depression Scale. They found that their “multi-stimulant approach” improved cognitive capacity among individuals older than 60 years.

In 2008 Huss et al. performed a meta-analysis that compared outcome data of older participants in preventive home visit programs with a control group [46]. They reviewed 21 randomized studies aimed at maintaining health and autonomy of older adults and preventing disability and subsequent nursing home admission. These studies also evaluated the impact of home visit programs on mortality, nursing home admissions, and functional status decline. The authors concluded that the preventive home visits have the potential to reduce disability among older adults when based on multidimensional assessment with clinical examination.

Approaches such as the “Functioning Improvement Tool Home-Visit Program (FIT-HVP)” are congruent with simple “naturalistic” assessment of everyday executive function in older adults. Such methods were tested McAlister et al. [47,48], who used the “Day-Out Task” (DOT). They described the DOT method as follows: “Participants were told to imagine that they were planning for a day out, which would include meeting a friend at a museum at 10: 00 am and later traveling to the friend’s house for dinner. The 8 subtasks that needed to be completed to prepare for the day out were then clearly explained and participants were provided with a detailed written list of the subtasks”. While participants were completing the DOT, 2 examiners, who were blind to group status, scored subtask accuracy and overall task accuracy. They state that the DOT is more suitable for the assessment of everyday functioning than cognitive tests are.

The procedures of cognitive training based on the intensification of family relations and advice provided during home visits are particularly desirable for treatment of “postoperative cognitive dysfunction” [49].

In journals devoted to sports medicine, some investigators often publish papers on the beneficial effects of physical exercise on cognitive capacity of older people. For instance, Torbejns et al. presented results of meta-analysis of studies related to the use of various types of equipment for physical exercises in work places [50]. They conclude that the implementation of active workstations might contribute to improving health and physical activity levels. Some authors emphasize that it is advantageous to combine physical exercise with cognitive activity [31,32,51]. We have already discussed other papers related to the importance of physical activity for mental capacity [28,29].

Parrott et al. stresses the importance of diet quality for maintaining cognitive performance [52], emphasizing that both diet quality and socioeconomic position have been linked to age-related cognitive changes. As the results of their investigations, they maintain that interventions promoting retention of cognitive function through improved diet quality would provide maximum benefit to those with relatively low socioeconomic position.

Attempt to Provide Practical Advice on Preventions and Treatment of Cognitive Impairments in Elderly

In the previous chapters we presented data to enable the reader to assess what has been achieved so far for gathering the arguments for the effectiveness of various methods of cognitive training and we have reviewed the various applicable cognitive intervention methods.

We would like to provide practical guidance on actions to prevent the decline of mental capacity in older people and trials attempting to improve the mental capacity (if it has already been impaired), especially in the form of “premature mild cognitive impairment” in the elderly.

Three possible goals should be distinguished: (1) Determine what actions elderly persons may already be taking, either alone or interacting with their doctor, nurse, or psychologist; (2) Determine what actions can be taken by health care institutions that desire to influence the health of a particular population; and (3) Determine the kinds of research that could be undertaken to improve the accessible methods.

The recommendations for individuals interested in preventing or correcting their own mental capacity result from the above-mentioned, tested and available methods. In short, we

can refer to: (a) Special computerized training methods mentioned by many of the above-cited authors [6–8,10,11]. The reader may become familiar with examples of such methods by delving into the generally available software tools listed in the Table 1; (b) Particular computer games that meet specific requirements [40–42]. Access to some of them is also indicated in the Table 1; (c) Structured guidance on the attitudes, behaviors, and learning methods [36,37,43,44,46–48].

Since we are considering taking action or providing assistance to the elderly, it should be noted that, due to already impaired mental capacity, it may be difficult for elderly to use computerized methods and to engage in the considerable mental effort required. In particular, it is difficult to ensure long-term use of these methods. Sometime, as in the course of treatment of “postoperative cognitive dysfunction”, use of computerized methods would be particularly inappropriate [49]. Therefore, we pay special attention to the possibility of recommending the enumerated (see “c”) structured guidance on the attitudes, behaviors, and learning methods.

However, when we consider the essence of these guidelines, it is easy to see that most of them merely recommend actions that promote being open, lively, interested, absorbing all kinds of positive stimuli from the outside world, and participating in various activities in the surrounding environment, including community activities.

This can be illustrated by general recommendations, which can be found on the page dedicated to the promotion of methods to improve mental health for people with dementia (see point 15 in the Table 1).

These recommendations are as follows: (1) Stay active mentally; (2) Be physically active; (3) Adopt a healthy diet; (4) Be an active member of the community, and (5) Take care of heart and other organs. We develop the topic “Stay active mentally” and recommend the following: (a) Be curious and engaged. Continue involvement in the workplace. Learn throughout life; (b) Read, write, solve crossword puzzles and jigsaw puzzles; (c) Attend lectures, readings, celebrations, and ceremonies; (d) Sign up for lectures (studies) in the nearby educational center (“university of the third age”) and colleges; (e) Sign up for 1 or 2 local groups targeted at self-help and self-development; (f) Play a variety of games such as chess, Go, and other board games or computer games; (g) Work in your backyard or community garden; (h) Try special methods of memory training; (i) Travel during weekends and holidays.

When we consider actions that may be taken by doctors, nurses, and psychologists involved in health promotion aimed at preventing mental impairment or helping those seeking to improve their mental capacity, it is necessary to undertake the

following activities: (1) It is necessary to be familiar with the latest experimental evidence of the relevance of various kinds of cognitive training and other interventions. The source of such information may be publications similar to this, our paper, together with the cited works. (2) It is necessary to organize a motivated, coherent, diligent, hard-working group that intends to undertake such actions and to ensure adequate funding or other forms of motivation for its action. (3) From the known methods of possible interventions, one should select a subset of diagnostic, preventive, and therapeutic methods specifically tailored to the purpose of the project to be undertaken. It is important to define the criteria that will be used to assess effectiveness, as well as the criteria for determining the circumstances in which we should refrain from project actions.

Regarding possible further research and clinical trials on methods of preventing and treating cognitive decline, we would like to quote the opinion expressed by Naqui et al. [1]. They wrote: “Future studies should address the impact of cognitive training on the prevention of cognitive decline, and encourage researchers to consider easily accessible tools such as crosswords puzzles and Sudoku, which have not been rigorously studied.”

This opinion stimulates us to realize how much remains to be done. The various tips listed above can be put into words, but the effectiveness of these tips has not yet been proven by objective investigations. In our opinion, different clinical trials are needed. For instance, it would be valuable to perform randomized, controlled clinical trials to compare the impact of various activities: 1. write an autobiography; 2. read a classic novel; 3. in older age, start to learn and play “contract bridge” (which is personally interactive), low-stakes poker (which promotes excitement), chess, or the most intellectual board game – GO. These are just a few examples.

We particularly believe that research is needed on the impact of activities such as the typical tourist trips in comparison to “therapeutic travel”. The concept of “traveling therapy” can be explained illustratively by the content of the article about the popular “wandering to Santiago de Compostela” [53].

There is also a significant challenge regarding methods to intensify sensual and sexual awareness and experience [54–56].

Simultaneously increasing cognitive and physical activities, as well as engaging in interpersonal interaction, appear to be the activities that most intensively affect the cognitive capacity of older people. Success in increasing interpersonal relations may, however, be hampered by isolation and loneliness, which are common in old age.

Our “practical advice” is in line with the concluding remarks of Kremen et al. [5]. They maintain that “intervention approaches” should ensure “social support, social engagement, cognitive activity, and reduction of stress” and that interventions should be “multimodal, multifaceted, integrated into everyday life, and targeted to vulnerable high-risk groups” [5].

Conclusions

1. Various methods of prevention and treatment of cognitive decline in the elderly have been investigated and verified in controlled clinical trials.
2. Mild cognitive impairment indicates increased risk of dementia, so it is important to establish precise procedures for the recognition of this clinical entity.

References:

1. Naqvi R, Liberman D, Rosenberg J et al: Preventing cognitive decline in healthy older adults. *CMAJ*, 2013; 185: 881–85
2. Salthouse T: Consequences of age-related cognitive declines. *Annu Rev Psychol*, 2012; 63: 201–26
3. Salgado JF, Anderson N, Moscoso S et al: A meta-analytic study of general mental ability validity for different occupations in the European community. *J Appl Psychol*, 2003; 88: 1068–81
4. Judge TA, Klinger RL, Simon LS: Time is on my side: time, general mental ability, human capital, and extrinsic career success. *J Appl Psychol*, 2010; 95: 92–107
5. Kremen WS, Lachman ME, Pruessner JC et al: Mechanisms of age-related cognitive change and targets for intervention: social interactions and stress. *J Gerontol A Biol Sci Med Sci*, 2012; 67: 760–65
6. Willis SL, Tennstedt SL, Marsiske M (ACTIVE Study Group) et al: Long-term effects of cognitive training on everyday functional outcomes in older adults. *JAMA*, 2006; 296: 2805–14
7. Jones RN, Marsiske M, Ball K et al: The ACTIVE cognitive training interventions and trajectories of performance among older adults. *J Aging Health*, 2013; 25(8 Suppl.): 186S–208S
8. Rebok GW, Ball K, Guey LT et al: Ten-year effects of the ACTIVE cognitive training trial on cognition and everyday functioning in older adults. *J Am Geriatr Soc*, 2014; 62: 16–24
9. Wolinsky FD, Mahncke H, Vander Weg MW et al: Speed of processing training protects self-rated health in older adults: enduring effects observed in the multi-site ACTIVE randomized controlled trial. *Int Psychogeriatr*, 2010; 22: 470–78
10. Smith GE, Housen P, Yaffe K et al: A cognitive training program based on principles of brain plasticity: results from the improvement in memory with plasticity-based adaptive cognitive training (IMPACT) study. *J Am Geriatr Soc*, 2009; 57: 594–603
11. Berry AS, Zanto TP, Clapp WC et al: The influence of perceptual training on working memory in older adults. *PLoS ONE*, 2010; 5: e11537
12. Burton CL, Strauss E, Bunce D et al: Functional abilities in older adults with mild cognitive impairment. *Gerontology*, 2009; 55: 570–81
13. Wadley VG, Okonkwo O, Crowe M, Ross-Meadows LA: Mild cognitive impairment and everyday function: evidence of reduced speed in performing instrumental activities of daily living. *Am J Geriatr Psychiatry*, 2008; 16: 416–24
14. Schmitter-Edgecombe M, Woo E, Greeley DR: Characterizing multiple memory deficits and their relation to everyday functioning in individuals with mild cognitive impairment. *Neuropsychology*, 2009; 23: 168–77
15. Lin JS, O'Connor E, Rossom RC et al: Screening for cognitive impairment in older adults: A systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med*, 2013; 159: 601–12
16. Wadley VG, Crowe M, Marsiske M et al: Changes in everyday function among individuals with psychometrically defined mild cognitive impairment in the ACTIVE Study. *J Am Geriatr Soc*, 2007; 55: 1192–98
17. Belleville S: Cognitive training for persons with mild cognitive impairment. *Int Psychogeriatr*, 2008; 20: 57–66
18. Faucounau V, Wu YH, Boulay M et al: Cognitive intervention programmes on patients affected by mild cognitive impairment: a promising intervention tool for MCI? *J Nutr Health Aging*, 2010; 14: 31–35
19. Li H, Li J, Li N et al: Cognitive intervention for persons with mild cognitive impairment: A meta-analysis. *Ageing Res Rev*, 2011; 10: 285–96
20. Panza F, D'Introno A, Colacicco AM et al: Current epidemiology of mild cognitive impairment and other predementia syndromes. *Am J Geriatr Psychiatry*, 2005; 13: 633–44
21. Marshall GA, Zoller AS, Kelly KE et al: Everyday cognition scale items that best discriminate between and predict progression from clinically normal to mild cognitive impairment. *Current Alzheimer Research*, 2014; 11: 853–61
22. Vlcek K, Laczo J: Neural correlates of spatial navigation changes in mild cognitive impairment and Alzheimer's disease. *Front Behav Neurosci*, 2014; 8: 89
23. Moser E, Moser MB: *Mapping Your Every Move*. Cerebrum, 2015; 2114: 4
24. Hasanein P, Shahidi S: Preventive effect of Teucrium polium on learning and memory deficits in diabetic rats. *Med Sci Monit*, 2012; 18(1): BR41–46
25. Akar F, Mutlu O, Celikyurt IK et al: Zaprinas and Rolipram enhances spatial and emotional memory in the elevated plus maze and passive avoidance tests and diminishes exploratory activity in naive mice. *Med Sci Monit Basic Res*, 2015; 21: 105–11
27. Celikyurt IK, Utkan T, Ozer C et al: Effects of YC-1 on learning and memory functions of aged rats. *Med Sci Monit Basic Res*, 2015; 21: 130–37
28. Cassilhas RC, Viana VA, Grassmann V et al: The impact of resistance exercise on the cognitive function of the elderly. *Med Sci Sports Exerc*, 2007; 39: 1401–7
29. Brown AK, Liu-Ambrose T, Tate R et al: The effect of group-based exercise on cognitive performance and mood in seniors residing in intermediate care and self-care retirement facilities: a randomised controlled trial. *Br J Sports Med*, 2009; 43: 608–14
30. Smith PJ, Blumenthal JA, Hoffman BM et al: Aerobic exercise and neurocognitive performance: a meta-analytic review of randomized controlled trials. *Psychosom Med*, 2010; 72: 239–52
31. Nouchi R, Taki Y, Takeuchi H et al: Beneficial effects of short-term combination exercise training on diverse cognitive functions in healthy older people: study protocol for a randomized controlled trial. *Trials*, 2012; 13: 200
32. Nouchi R, Taki Y, Takeuchi H et al: Four weeks of combination exercise training improved executive functions, episodic memory, and processing speed in healthy elderly people: evidence from a randomized controlled trial. *Age (Dordr)*, 2014; 36: 787–99

33. Belleville S, Bherer L: Biomarkers of cognitive training effects in aging. *Curr Transl Geriatr Exp Gerontol Rep*, 2012; 1: 104–10
34. Thompson TW, Waskom ML, Garell KL et al: Failure of working memory training to enhance cognition or intelligence. *PLoS One*, 2013; 8(5): e63614
35. Ackerman PL, Kanfer R, Calderwood C: Use it or lose it? Wii brain exercise practice and reading for domain knowledge. *Psychol Aging*, 2010; 25: 753–66
36. Nouchi R, Taki Y, Takeuchi H et al: Beneficial effects of reading aloud and solving simple arithmetic calculations (learning therapy) on a wide range of cognitive functions in the healthy elderly: study protocol for a randomized controlled trial. *Trials*, 2012; 13: 32
37. Kawashima R, Okita K, Yamazaki R et al: Reading aloud and arithmetic calculation improve frontal function of people with dementia. *J Gerontol A Biol Sci Med Sci*, 2005; 60: 380–84
38. Osaka M, Otsuka Y, Osaka N: Verbal to visual code switching improves working memory in older adults: an fMRI study. *Front Hum Neurosci*, 2012; 6: 24
39. Osaka M, Yaoi K, Otsuka Y et al: Practice on conflict tasks promotes executive function of working memory in the elderly. *Behav Brain Res*, 2012; 233: 90–98
40. Nouchi R, Taki Y, Takeuchi H et al: Brain training game improves executive functions and processing speed in the elderly: a randomized controlled trial. *PLoS One*, 2012; 7: e29676
41. Rainville C, Lepage E, Gauthier S et al: Executive function deficits in persons with mild cognitive impairment: a study with a Tower of London task. *J Clin Exp Neuropsychol*, 2012; 34: 306–24
42. Peretz C, Korczyn AD, Shatil E et al: Computer-based, personalized cognitive training versus classical computer games: a randomized double-blind prospective trial of cognitive stimulation. *Neuroepidemiology*, 2011; 36: 91–99
43. Ukawa S, Satoh H, Yuasa M et al: A randomized controlled trial of a Functioning Improvement Tool home-visit program and its effect on cognitive function in older persons. *Int J Geriatr Psychiatry*, 2012; 27: 557–64
44. Ukawa S, Yuasa M, Ikeno T et al: Randomised controlled pilot study in Japan comparing a home visit program using a Functioning Improvement Tool with a home visit with conversation alone. *Australas J Ageing*, 2012; 31: 187–89
45. Karatay G, Akkuş Y: The effectiveness of a stimulation program on cognitive capacity among individuals older than 60. *West J Nurs Res*, 2011; 33: 26–44
46. Huss A, Stuck AE, Rubenstein LZ et al: Multidimensional preventive home visit programs for community-dwelling older adults: a systematic review and meta-analysis of randomized controlled trials. *J Gerontol A Biol Sci Med Sci*, 2008; 63: 298–307
47. McAlister C, Schmitter-Edgecombe M: Naturalistic assessment of executive function and everyday multitasking in healthy older adults. *Neuropsychol Dev Cogn B Aging Neuropsychol Cogn*, 2013; 20: 735–56
48. Schmitter-Edgecombe M, McAlister C, Weakley A: Naturalistic assessment of everyday functioning in individuals with mild cognitive impairment: the day-out task. *Neuropsychology*, 2012; 26: 631–41
49. Wang W, Wang Y, Wu H et al: Postoperative cognitive dysfunction: Current developments in mechanism and prevention. *Med Sci Monit*, 2015; 21: 1908–12
50. Torbeyns T, Bailey S, Bos I, Meeusen R: Active workstations to fight sedentary behaviour. *Sports Med*; 2014; 44(9): 1261–73
51. Langdon KD, Corbett D: Improved working memory following novel combinations of physical and cognitive activity. *Neurorehabil Neural Repair*, 2012; 26: 523–32
52. Parrott MD, Shatenstein B, Ferland G et al: Relationship between diet quality and cognition depends on socioeconomic position in healthy older adults. *J Nutr*, 2013; 143: 1767–73
53. Moreno J: Pilgrims Inc.: Soul Searching and Commerce on the Way of St. James <http://www.spiegel.de/international/europe/more-popular-than-ever-way-of-st-james-still-offers-enlightenment-a-983670.html>
54. van Lankveld JJ, Geijen WE, Sykora H: The sexual self-consciousness scale: psychometric properties. *Arch Sex Behav*, 2008; 37: 925–33
55. Toledano R, Pfaus J: The Sexual Arousal and Desire Inventory (SADI): a multidimensional scale to assess subjective sexual arousal and desire. *J Sex Med*, 2006; 3: 853–77
56. Clayton AH, Segraves RT, Leiblum S et al: Reliability and validity of the Sexual Interest and Desire Inventory-Female (SIDI-F), a scale designed to measure severity of female hypoactive sexual desire disorder. *J Sex Marital Ther*, 2006; 32: 115–35