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Effectiveness of Computerized Cognitive Training in Preventing Cognitive Decline in Older Adults with Mild Cognitive Impairment

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I. Background

Mild cognitive impairment (MCI) relates to cognitive decline from a previous level of functioning, both by subjective and objective evidence. Different clinical criteria can be applied to identify people with MCI and, according to the definition used, its prevalence estimates may vary from 5.0% to 36.7% and they increase with the population age [1].

In broad terms, the level of cognitive decline associated with MCI is greater than expected for age, but not as severe as that associated with dementia, with minimal impairment of Instrumental Activities of Daily Living (IADL) [2].

MCI increases the risk for dementia, with diagnosed individuals progressing at rates up to 6-10% per year compared with 1-2% in the general population [3].

The major MCI subtypes are amnestic (aMCI), involving episodic memory impairment (with or without impairment in other cognitive domains), and non-amnestic (na-MCI), involving impairment in cognitive domains other than memory (e.g. language, visuospatial processing, executive functions).

From a healthcare perspective, the higher prevalence of this age-related impairment in cognitive functions and the contemporary expanding aging population highlight the need to identify quick, effective and low-cost solutions to delay pathological cognitive decline [4].

Successfully assisting older adults to possibly slow cognitive decline, maintaining quality of life and independence, remains indeed a major challenge [5].

Since the relative pharmacological treatment ineffectiveness to face this problem [2], there has been a growing interest in the potential for lifestyle interventions, such as appropriate mental activities, to improve or maintain the cognitive functions.

To this purpose, cognitive training is a specific form of non-pharmacological intervention to address cognitive and non-cognitive outcomes [6]. It involves guided practice on a set of standardized tasks that aim to address specific aspects of cognition, such as memory, language, attention or executive functions.

Within the different tasks, varying difficulty levels may be offered to continuously adjust task difficulty based on the subjects performance [7].

Traditional training programs are usually delivered in groups or face-to face, which entails identifying a convenient meeting location, coordinating schedules and travel time. To overcome these aspects, novel cognitive training platforms have been developed and structured recently and, in this context, computer-based cognitive interventions are becoming a potentially cost-effective alternative to traditional training forms.

Firstly, they can be easily disseminated, reaching special populations that would otherwise not receive such interventions (e.g. older adults who have limited access to transportation are difficult to recruit for traditional cognitive training programs); secondly, they can offer a more flexible, personalized approach to anyone with access to technology; thirdly, they can provide real-time performance feedbacks to all the users.

Lastly, poor adherence can be a challenge with traditional cognitive training programs. In contrast, computer and video games are designed to be fun and exciting and may provide motivation for older adults to stick with the training program [4].

In this research, given the extensive body of data reporting whether older adults can benefit from cognitive training interventions, we specifically focused on the effectiveness of computerized cognitive training in people with mild cognitive impairment to summarize the main available evidence on the topic.

II. Searching for evidence

Methodology

The search process was carried out in three steps.

In step one, we used the PICO strategy to identify the search terms and the research question. PICO represents an acronym for Patient, Intervention, Comparison and Outcome. These four components are the essential elements of the question construction for the bibliographic search of available data.

In particular, we focused on the scientific evidence about the effectiveness of computerized cognitive training in older adults with MCI.

In step two, we conducted a literature review using the main electronic databases Medline and Scopus.

Search terms previously identified and used were "cognitive training" OR "brain training" OR "computerized cognitive training" AND "mild cognitive impairment" OR "MCI" OR "cognitive decline".

The literature search was performed and updated through March 2018.

Eligible studies were published in English or Italian, peer reviewed reports of randomized controlled trials (RCTs), systematic reviews or meta-analyses, evaluating the effects of computer-based cognitive training on people with MCI or with early-stage dementia.

After screening the titles and abstracts, we identified a recently published meta-analysis (2017) which addressed all the essential elements of our research question [8].

In particular, it is a systematic review of the effectiveness of computerized cognitive training in older adults with mild cognitive impairment with a statistical analysis of its effects on global cognition and on the individual cognitive domains, useful to chart potential benefits on cognition and behavior across the distinct domains.

It includes only RCTs published from databases inception to 1st July 2016.

In step three, we extracted and analyzed all the relevant data from the articles which were included in the meta-analysis and we specifically searched the literature for the latest articles to update it.

To our knowledge, no new articles were published from 1st July 2016 to 15th March 2018 that were relevant for our research.

Results

a) Characteristics of Included Studies

The meta-analysis authors screened more than 22,200 records to finally include 16 articles: 14 published in English, one in German and one in Korean which were translated before being analyzed. Two were split into two studies each [9], [10], and two articles reporting outcomes from the same trial were combined into one study [11], [12], resulting in a final data set of 17 independent comparisons included and analyzed (see Annex 1, Table 1).

The total number of participants was 686 (Computerized Cognitive Training group: N=351, mean group size: N=21; Control: N=335, mean group size: N=20). Mean age ranged between 67 and 81 years.

Active control, defined as sham CCT or psychoeducation, was reported in 11/17 studies.

In the remaining studies, passive activities (e.g. no-contact, wait-list) were offered to the control arm.

Studies combining CCT with other interventions were eligible if the control group received the same adjacent intervention.

All the articles were assessed using the PEDro-P scale, a critical appraisal to determine the methodology quality of clinical trials. The reported mean PEDro-P score was 7.2/9 (SD=1.03).

Each computer-based session in the cognitive training group lasted from 20 minutes to a maximum of 100, with a mean length of 63.5 minutes. The mean number of sessions performed by the experimental group was 29.9, with a mean of 2.59 session per week.

Baseline cognitive characteristics of participants undergoing the cognitive training were examined for most studies using the Mini-Mental State Examination (13/17) with a mean score ranging from 22.88 to 27.79.

b) <u>Program Description and Program-Targeted Cognitive Domains</u>

There are many different available tools for cognitive training and specific structured software designed for it.

Particularly, most of the studies included in this meta-analysis (11/17) used exercises from structured software programs that were planned to become progressively more difficult at each session and adjustable according to user performance (so that each person is always training at the higher level).

The software packages used are: Cogpack®, Brainfitness and InSight by Posit Science, Sociable, Lumosity Inc., CogniPlus Training Program and Nintendo Wii.

A brief description of each software is reported below:

- Cogpack® [9] consists in 64 tests and training programs with 537 different task sets, e.g. for visuomotor control, comprehension, reaction, vigilance, memory, language, numbers, logic, problem solving, knowledge, orientation, everyday skills, intellectual and professional skills and other special elements (e.g. labyrinths, color/word interference, 3-D positioning and assumptions about public opinion). Tasks can be edited, changed, and expanded.
- Brainfitness by Posit Science [5], [10] focuses on the auditory system of the brain, recognizing to the speech a central role. It consists in 6 easy-to-use and computer-based exercises that improve the auditory system in several ways, as speeding up processing, clarifying sound discrimination, sharpening sound precision, improving sound sequencing, strengthening auditory working memory and enhancing narrative memory.
- InSight by Posit Science [13] targets key roots of cognitive function (the brain's ability to take information from the senses quickly and accurately) in addition to exercising memory directly. It consists of 5 games designed to improve the visual system, and particularly: speeding up visual processing, sharpening visual precision, enlarging useful field of view, expanding divided attention and improving visual working memory.
- Lumosity Inc. [14] is a free on-line website designed to train cognitive, math and language skills. A set of 3 games is offered daily, always adjusted to user performance and skill level.

- Sociable [15] is a platform that offers personalized cognitive training, covering all the cognitive skills, focusing on memory, orientation, attention, constructural praxis, executive functions, language and logical reasoning. Sociable boosts the social interactions of the elderly and motivates them by selected game concepts and themes.
- CogniPlus [11], [12] is a training battery for the training of cognitive functions. Each CogniPlus training is tailored to a specific deficit, which is scientifically proven to be trainable. The domains are: attention, memory, executive functions, spatial processing, visuomotor skills and processing speed. In CogniPlus the ability dimensions being trained are almost always embedded in lifelike scenarios.
- Nintendo Wii is a game where participants are trained to use their arms/body to simulate the actions required for each sport. It was used in two different studies; in the first study [16] only Nintendo Wii bowling was used, while the other one [17] used Nintendo Wii sports (which includes bowling, golf, tennis and baseball).

The other cognitive interventions included in the meta-analysis did not refer to any specific software program, but the authors described the exercise types.

In particular, one study [18] used "repetition lag-training" tasks which required the learning of a series of words and the discrimination of those words from unstudied lures. Three studies used virtual reality tasks; one for simulating museum tasks [19], one for simulating household tasks [20] and one for simulating a bike ride [21].

The remaining studies [22], [23] used other types of exercise (e.g. memorizing and recognizing pictures, correlating words semantically, solving puzzle).

In general, during a CCT session, 4 or 5 exercises were administered to participants in the CCT groups.

Most of the tasks that participants had to carry out involved attention domain (11/17), executive functions (10/17), memory (verbal (8/17) and nonverbal/visual (7/17)), followed by speed processing (6/17) and visuospatial processing (5/17).

a) Overall efficacy on Cognitive Outcomes

Standardized mean differences and their 95% confidence interval of change in cognitive outcomes measures were calculated between the CCT group and the control group, from baseline to post-training.

A positive standardized mean difference indicates a therapeutic effect of CCT over and above the control (Fig. 1).

Different tests were used to measure the cognitive outcome across the studies. A list of the results categorized by the cognitive domain is reported below.

- Global cognition

  The effect of CCT on global cognition was measured in 12/17 studies and it was found to be moderate and statistically significant. There was no difference between the effect across active or passive controlled trials.
- Verbal learning

  The effect of CCT on verbal learning was measured in 3/17 studies and it was found to be moderate and statistically significant.
- Verbal memory

The effect of CCT on verbal memory was measured in 7/17 studies and it was found to be moderate and statistically significant.

- Nonverbal learning

  The effect of CCT on nonverbal learning was measured in 8/17 studies and it was found to be moderate and statistically significant.

- Working memory

  The effect of CCT on working memory was measured in 9/17 studies and it was found to be large and statistically significant.

- Attention

  The effect of CCT on attention was measured in 11/17 studies and it was found to be moderate and statistically significant.

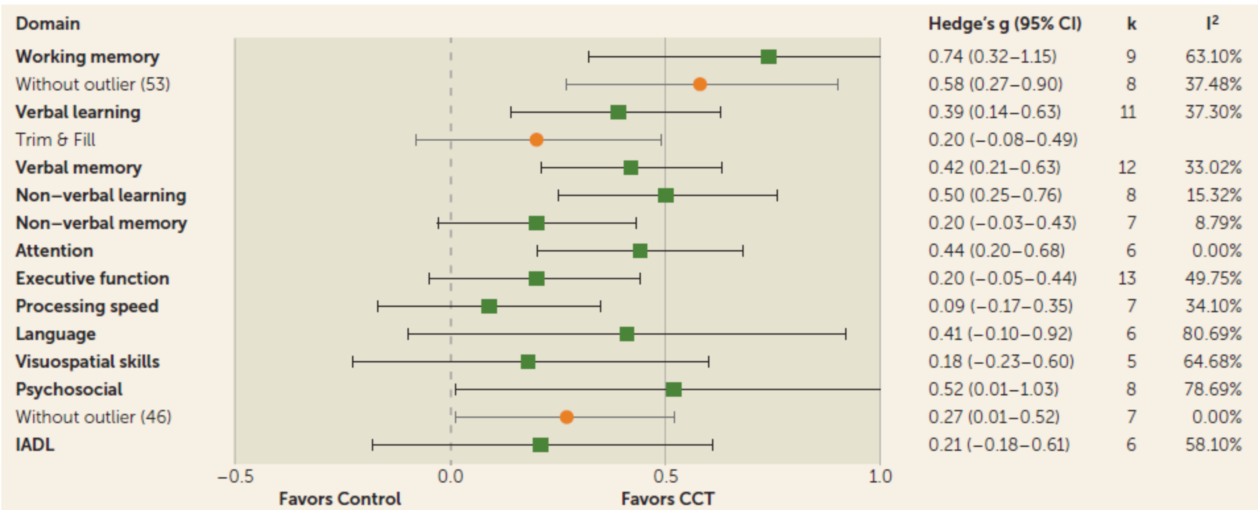
- Psychosocial functioning

  The effect of CCT on psychosocial functioning was measured in 8/17 studies and it was found to be moderate and statistically significant.

- Other domains

  Statistically non-significant results were found for nonverbal memory, executive functions, processing speed, visuospatial skills, language or Instrumental Activities of Daily Living (IADL).

Fig. 1. Efficacy of Computerized Cognitive Training (CCT) in people with mild cognitive impairment within individual domains.



III. Conclusions

Based on the results of 17 randomized controlled trials of moderate quality, CCT is an effective intervention for enhancing cognition in people with mild cognitive impairment.

In particular, participants in CCT groups improved significantly over the intervention period, while controls did not show any cognitive change, as it was found in the global cognition domain. Most of the trials used (70%) used an active control condition, but the effects across active- and passive-controlled trials were comparable.

In addition, moderate effect sizes on most memory and learning domains were relevant.

Also attention, defined as a behavioral and cognitive process of selectively concentrating on a discrete aspect of information while ignoring perceivable information, significantly benefited from the computer-based training.

On the other hand, CCT lacked of efficacy on executive functions but, since cognitive training gains typically reflect training content, this result may be due to insufficient training on executive processes (mainly fluid intelligence, inhibitory control and reasoning) within studies.

Surprisingly, the effects of CCT on speed and visuospatial processing were found to be statistically not significant even though CCT exercises are typically timed and involved visuospatial skills. Moreover, these domains were among the most responsive in other meta-analyses on healthy adults and patients with Parkinson disease.

Again, changing the training content and focusing specifically on processing speed and visuospatial may improve this result.

Depression is associated with mild cognitive impairment. Notably, psychological functioning (depression, quality of life and neuropsychiatric symptoms) showed a positive improvement after the CCT training and this suggests that CCT may also benefit general mood.

Reliable effects were not seen on Instrumental Activities of Daily Living (IADL) and language outcomes, but relatively few studies investigated these domains.

In conclusion, CCT is efficacious on global cognition, memory, working memory and attention and helps improve psychological functioning, including depressing symptoms, in people with mild cognitive impairment.

These results are robust and indicate a beneficial therapeutic role for CCT in this population and, since the many advantages that it offers, it should be considered as a cost-effective tool to prevent cognitive decline and to maintain quality of life and independence in older people.

IV. Conflict of interests and funding

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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VI. Annexes

Table 1. Characteristics of Included Studies[a]

Study	N and Control Type	Mean Age (Years)[b]	Mean MMSE or Equivalent	Program Description	Program-Targeted Cognitive Domains	Session Lenght (minutes)	Sessions/ Week	Total Training (hours)	PEDro-P Scale
Kim et al. [20]	CCT N=15 Control (Active) N=15	78.7	26.7	**Unspecified software** Participants were practiced in performing household tasks using virtual reality.	-	30	3	6	7
Rozzini et al. [22]	CCT N=15 Control (Active) N=22	-	26.2	**Unspecified software** - Memory: participants were trained in recognition tasks for word lists, images and sequences of items; - Attention: participants were practiced in responding at the presentation of a target or in recognizing and choosing among different possibilities the two images-targets presented simultaneously; - Language: participants were exercised in correlating words semantically and in perceiving different images or associating couples of figures; - Visuo-spatial: participants were practiced in solving puzzles, visual search tasks and location of visual information.	- Verbal memory - Nonverbal memory - Attention - Language - Executive functions - Visuospatial processing	60	5	60	8
Barnes et al. [24]	CCT N=22 Control (Active) N=25	74	-	**BrainFitness by Posit Science** The program involved 7 exercises that were designed to improve processing	- Processing speed - Verbal memory - Working memory	100	5	50	8

				speed and accuracy; primary and working auditory memory tasks were woven implicitly into the exercises.					
Finn et al. [14]	CCT N=8 Control (Passive) N=8	72.69	27.76	**Lumosity Inc.** Exercise types: - Birdwatching - Color match - Lost in migration - Memory match - Raindrops - Spatial speed match	- Attention - Processing speed - Nonverbal memory - Executive functions	20	3-5	10	7
Herrera et al. [23]	CCT N=11 Control (Active) N=11	76.63	27.27	**Unspecified software** Exercise types: - <u>Visual recognition:</u> participants were asked to memorize and recognize pictures, with or without a distractor; - <u>Visuospatial recognition:</u> participants were asked to memorize objects positions and recognize this layout; - <u>Visual recognition/working memory:</u> participants were asked to memorize pictures old and new and continuously recognize them; - <u>Visual focused attention:</u> participants were asked to detect a target picture; - <u>Visuospatial focused attention:</u> participants were asked to recognize and detect a target picture in different screen parts; - <u>Divided attention (trial):</u> participants were asked to recognize pictures	- Verbal memory - Nonverbal memory - Verbal learning - Nonverbal learning - Attention - Processing speed	60	2	24	8

				that corresponded to words heard among distractors.					
Tarnanas et al. [19]	CCT N=32 Control (Active) N=39	70.05	26.5	**Unspecified software** Participants were practiced in performing museum tasks using virtual reality.	-	90	2	60	7
Wittelsberger et al. [16]	CCT N=17 Control (Passive) N=10	70.07	22.88	**Nintendo Wii bowling**	-	60	2	12	5
Finn et al. [18]	CCT N=12 Control (Passive) N=12	73.95	27.79	**Unspecified software** Participants were asked to learn a series of words and subsequent discriminate those words from unstudied lures.	- Verbal learning - Verbal memory	90	2	9	6
Hughes et al. [17]	CCT N=10 Control (Active) N=10	77.4	27.1	**Nintendo Wii sports**	-	90	1	36	7
Fiatarone Singh et al. (study 1) [9]	CCT N=27 Control (Active) N=22	70.1	27	**Cogpack**	- Verbal memory - Nonverbal memory - Executive functions - Attention - Processing speed	90	2	78	9
Fiatarone Singh et al. (study 2) [9]	CCT N=24 Control (Active) N=27	70.1	27	**Cogpack**	- Verbal memory - Nonverbal memory - Executive functions - Attention - Processing speed	90	2	78	9
Barban et al. [15]	CCT N=46 Control (Passive) N=60	73.54	27.74	**Sociable** Exercise types: - Episodic memory: participants were asked to remember a list, to remember object locations in	- Verbal memory - Nonverbal memory - Executive functions - Language - Attention	60	2	24	8

				domestic environments and to find pairs of images; - Attentional Executive Functions: participants were asked to selectively pay attention to stimuli avoiding distractors, to abstract, to explain similarities, to categorize objects, to deduct a target by excluding the distractors; - Orientation: participants were asked to move into a house; - Logical reasoning: participants were asked to compare a visual pattern with a missing element; - Constructional praxis: participants were asked to do a puzzle; - Language: participants were asked to couple synonyms or antonyms.	- Visuospatial processing				
Hagovska et al. [11] [12]	CCT N=40 Control (Passive) N=38	66.97	26.33	**CogniPlus** - Attention intensity “Alert”: driving a car - Long-term memory “Names”: remembering names and surnames in connection with faces - Executive functions “Pland”: solving tasks - Working memory “Nback”: remembering two or three pictures previously presented through time - Visual-motor coordination “Vismo”: following a spaceship on the screen and keeping it inside a circle - Each exercise featured up to 28 progressive difficulty levels	- Verbal memory - Nonverbal memory - Verbal learning - Nonverbal learning - Working memory - Executive functions - Attention - Visuospatial processing	30	2	10	7

				adjustable according to users performance.					
Barcelos et al. [21]	CCT N=8 Control (Active) N=9	80.6	20.8[c]	**Unspecified software** Participants were trained to ride virtual reality enhanced and recumbent stationary bikes through a scenic landscape, where they were instructed to collect different colored coins and corresponding colored dragons.	- Executive functions - Attention - Visuospatial processing	20-45	2	18	6
Gooding et al. (study 1) [10]	CCT N=31 Control (Active) N=20	75.59 [j]	50.62[d]	**BrainFitness by Posit Science**	- Memory - Attention - Executive functions	60	2	30	5
Gooding et al. (study 2) [10]	CVT N=23 Control (Active) N=20	75.59[j]	50.84[d]	**BrainFitness by Posit Science**	- Memory - Attention - Executive functions	60	2	30	5
Lin et al. [13]	CCT N=10 Control (Active) N=11	73.0	25.02[c]	**InSight by Posit Science** Exercise types: - Eye for details - Peripheral challenge - Visual sweeps - Double decisions - Target tracker	- Processing speed - Visuospatial processing - Executive functions - Attention	60	4	24	7

[a] Abbreviations: CCT= Computerized Cognitive Training; CVT= Cognitive Vitality Training; PED-ro P= Physiotherapy Evidence Database Rating Scale.

[b] Weighted mean age.

[c] Measured using the Montreal Cognitive Assessment (1-30 scale).

[d] Measured using the Modified Mini-Mental State Examination (1-100 scale).

[e] Summary statistics from study 1 and study.