

Approaches to Cognitive Stimulation in the Prevention of Dementia

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Abstract

The prevalence of dementia and age-related cognitive impairment is rising due to an aging population worldwide. There is currently no effective pharmacological treatment, but cognitive activity programs could contribute to prevention and risk reduction. However, the results of intervention studies are inconclusive, which may be related to methodological issues. For example, the inconsistent use of umbrella categories to describe cognitive intervention strategies, such as cognitive training or cognitive rehabilitation, has led to confusion regarding their respective contents and efficacies. The interventions studied so far draw on a pool of common basic ingredients. Therefore, rather than focusing on a few high-level categories, it might be beneficial to examine the efficacy of more basic cognitive intervention ingredients, which form the building blocks of complex multi-strand cognitive intervention strategies. Here we suggested a novel format of collating basic cognitive intervention ingredients. Using a representative sample of review articles and treatment studies, we attempted to inventory the most commonly encountered ingredients. Finally, we discuss their suitability for individualized and group-based approaches, as well as the possibility for computerization.

Keywords: Dementia; Cognitive stimulation; Brain

Abbreviations:

AD: Alzheimer's Disease; ADL: Activities of Daily Living; B/A: Before and After study; BAR: Brain-Activating Rehabilitation; CAT: Computer-Assisted Cognitive Training Program; CCS: Case Control Study; CMI: Cognitive-Motor Intervention; CR: Cognitive Rehabilitation; CST: Cognitive Stimulation Therapy; ELSA: English Longitudinal Study of Aging; HVL: Hopkins Verbal Learning Test; IADL: Instrumental Activities of Daily Living; ICT: Interactive Computer-Based Cognitive Training; IMIS: Interactive Multimedia Internet-Based System; IPS: Information Processing Speed; LSS: Lexical Semantic Stimulation; MAK: Motor Stimulation (M), ADL (A), Cognitive Stimulation (K), Spiritual Element (S); MCI: Mild Cognitive Impairment; MMSE: Mini Mental State Examination; MoCA: Montreal Cognitive Assessment; MOOC: Massive Open Online Courses; MS: Mental Stimulation; NPT: Neuro Psychological Training; NRCT: Non-Randomized Controlled Trial; RAVLT: Rey Auditory Verbal Learning Test; RCT: Randomized Controlled Trial; ROT: Reality Orientation Therapy; TMT: Trail Making Test (level A (numbers only) and level B (numbers and letters)); TNP: Training Neuro-Psychological (software)

Introduction

Dementia and age-related cognitive decline have shown an increase due to an aging population worldwide and treatments to target prevention of cognitive decline are sorely needed. Activity programs to improve or maintain cognitive function may hold some promise. However, research into the efficacy of cognitive intervention strategies targeting cognitive decline has generated contradictory results. Confusion and discrepancies are largely due to methodological

shortcomings. There is, for example, no clear and well-defined nomenclature describing cognitive intervention strategies. While there have been attempts at theoretically categorizing cognitive intervention strategies into 'training', 'rehabilitation', and 'stimulation', this distinction is hard to enforce in practice [1]. Most interventions comprise aspects or 'ingredients' of at least two out of the three categories, while the categories themselves are poorly defined and used inconsistently throughout the literature [1]. In addition, there have been numerous calls for the introduction of further categories, such as 'cognitive recreation', to describe the use of computerized technology as part of cognitive interventions, adding to the existing confusion pertaining to the categorization of cognitive intervention strategies. As a corollary, statements regarding the content or efficacy of cognitive intervention strategies are questionable.

A focus on the identification and appraisal of active ingredients would avert the issue of categorization altogether. For example, one may classify interventions more specifically as 'reality orientation therapy' or 'method of loci', rather than 'cognitive training'. The effective identification of these ingredients is, however, often hindered by the incomplete description of intervention protocols. Access to intervention protocols is not only essential for the identification of intervention ingredients, but also for the replication and validation of reported effects. Intervention protocols should therefore routinely be made available to the scientific community in the form of online supplements or attachments. Here, we attempted to identify such active ingredients with the aim of providing a foundation for the systematic appraisal of their efficacy in delaying or preventing cognitive decline and dementia.

Methods

We examined a representative sample of review articles published in English in peer-reviewed journals published between 2010-2016, which investigated cognitive interventions for people with mild cognitive impairment (MCI) or dementia. We also studied individual treatment studies. This was not a systematic review, but rather a scoping exercise to develop novel categories and ingredients, which could be useful for a systematic review of this vast literature of cognitive interventions for cognitive impairment. Therefore, the sample is not exhaustive. Pharmacological interventions for dementia and MCI, neurological or biological factors and reviews focusing on caregivers only were excluded. In total, 22 [1-21] reviews and 36 treatment study articles (Table 1) [22-57] were screened.

Contents of the cognitive intervention protocols were examined and the individual ingredients comprised therein were identified. An

overview of the effort to identify the active intervention ingredients is presented in Table 1. A similar list of active cognitive intervention ingredients has previously been published by Simon et al. [19]; however, the review by Simon et al. [19] focused on compensatory and restorative strategies for treatment of amnesic MCI patients only. Here we also investigated treatments for dementia and extended the list with additional cognitive intervention ingredients identified in the literature. Based on the review by Simon et al. [19] and our own literature search we collated a number of ingredients which can be clustered in the categories listed below. Most interventions had a minimum of two ingredients for which there was some scientific evidence base of efficacy (i.e. they had a positive treatment effect on cognition, mood and/or activities of daily living (ADL)).

Citation	Design	Type of intervention	Intervention Details	Delivery	Treatment group	Computer delivery
Barnes [22]	RCT	3 types of computer activities, cognitive training performed at participants' homes	The program involved 7 exercises, which were designed to improve auditory processing speed and accuracy in the auditory cortex; primary and working auditory memory tasks.	individual	22 MCI	yes
Belleville [23]	NRCT	Group training with tutors	Group training (4-5), three instructors (clinical neuropsychologists), Session 1: outline of program; Sessions 2+3: computer-assisted attentional training (e.g. divided attention); learning through tutoring and observation; use of "fading techniques" in which the instructor provided decreasing support and cues to the participants. Teaching episodic memory strategies.	group	31 mixed MCI and healthy elderly	mixed
Brum [24]	RCT	Cognitive training in older adults with MCI	The training protocol applied to patients involved an educational component on memory and aging, and a practical component on cognitive tasks. The aim of the protocol was to implement the compensatory strategy (categorization) for episodic memory tasks through ecologic activities which simulated activities of daily living. The training also included tasks involving executive functions by means of simulated tasks of giving and checking change.	1	16 MCI	
Buschert [25]	RCT	Amnesic MCI received cognitive training of specific domains (e.g. memory function) as well as cognitive stimulation; Alzheimer's disease patients received cognitive stimulation	Educational information regarding meta-cognition (e.g. information processing), age-associated decline, and cognitive changes in AD was provided; reminiscence therapy, psychomotor and recreational tasks, encouragement of social interactions; teaching and practicing restorative and compensatory mnemonic strategies, activation of intellectual and physical leisure activities; training perception, attention, and memory.	group	12 amnesic MCI 7 AD	no

Buschert [26]	RCT	Multicomponent cognitive group intervention	Teaching and training mnemonics, memory techniques, as well as cognitive and social informal engagement.	group	10 MCI	no
Cipriani [27]	NRCT	Computerized Neuropsychological Training (NPT)	Software includes exercises stimulating attention, memory, perception, visuospatial cognition, language, and non-verbal intelligence.	individual	10 MCI 10 AD	yes
Clare [28]	RCT	Cognitive rehabilitation	The intervention consisted of personalized interventions to address individually relevant goals supported by components addressing practical memory aids and strategies, techniques for learning new information, practice in maintaining attention and concentration, and techniques for stress management.	individual	24 AD and MCI	no
Coen [29]	RCT	Cognitive stimulation therapy	Training targeted psychological and social abilities that influence cognition such as self-confidence, motivation and the feeling of belonging. Cognitive functions are addressed by using practical everyday situations and tasks, such as recognizing famous faces, playing word games, reading facial expressions, and discussing relevant themes such as food and money. Themes include physical games, sound, childhood, food, current affairs, faces/scenes, word association, being creative, categorizing objects, orientation, using money, number games, word games, team quiz.	group	14 AD	no
Fernandez-Calvo [30]	RCT	1) Big Brain academy (cognitive training game) 2) Psychostimulation Program	Big Brain academy is a game on the Wii platform that aims to stimulate mental capacity, such as perception, memory, calculations, analytical, visual recognition;	individual	15 AD	yes
Filipin [31]	Retrospective Cohort Study	Cognitive stimulation	Group activities which aimed to enhance cognitive and functional activities. It included various topics such as word association, object categorization, visual imaging, discussion of current affairs, orientation and executive control training techniques.	group	42 mixed MCI and AD	no
Gagnon [32]	RCT	Cognitive intervention for attentional control	The experimental group completed a computer-based training program involving Variable Priority coordination of both components of a dual task, to which a self-regulatory strategy to augment meta-cognition was added. The active control group performed Fixed Priority training: rote practice of the same dual task involving a visual detection task combined with an alpha-arithmetic task.	individual	12 MCI	yes
Galante [33]	RCT	Cognitive rehabilitation	Computer exercises for: memory, language, perception, intelligence, attention, memory, perception, spatial cognition.	individual	7 MCI and AD	yes

Giuli [34]	RCT	Comprehensive training	Objective of training: teach compensatory techniques (e.g. mnemonics); learning strategies of categorization, clustering attention, and visuospatial processes; decrease functional disability, engage in ADL	Individual for MCI and AD; group for healthy participants.	160 mixed AD, MCI and without cognitive decline	no
Graessel [35]	RCT	Cognitive stimulation	MAKS (motor stimulation, practice in activities of daily living, and cognitive stimulation)	groups	31 mixed elderly, AD	no
Günther [36]	B/A	Computer-assisted cognitive training program (CAT)	The study used 'Cognition I' (version 3.93), which includes exercises that are designed to increase attention, visuo-motor performance, reaction time, vigilance, attentiveness, memory, verbal performance and general knowledge.	individual	19 non-demented elderly with memory impairment	yes
Hofmann [37]	CCS	Interactive computer-based cognitive training (ICT)	Computer-based training simulating a shopping route, including social competence tasks and tests of orientation and memory.	individuals	9 AD	yes
Jelcic [38]	RCT	Lexical semantic stimulation (LSS)	Lexical-semantic rehabilitation exercises; lexical tasks aimed at enhancing semantic verbal processing;	groups	20 AD	no
Jelcic [39]	RCT	2 types of LSS: 1) Teleconference with therapist; lexical tasks, word interpretation, sentences and stories (LSS tele). 2) LSS direct: therapist provides treatment.	The LSS protocol contained lexical tasks aimed at enhancing semantic verbal processing. The exercises focused on the interpretation of written words, sentences, and stories; interventions were delivered by trained therapists either face to face or via Skype	individual	7 AD	video call
Konsztowicz [40]	RCT	Memory training	Training in selective attention, visual imagery skill and mnemonic strategies. Memory compensation, aimed at promoting independent living, teaches organizational strategies and procedural learning; set up a memory support system for everyday use, use of memory book.	group	8 in memory training; 7 in memory compensation. All MCI.	no
Kounti [41]	RCT	Cognitive training and rehabilitation through kinetic exercises	Enhance visual and auditory, selective attention, shifting, and switching of attention, and dual-task; indirect teaching of learning strategies; contains visuomotor and verbal-kinetic stimuli.	group	29 MCI	no
Kurz [42]	B/A	Cognitive rehabilitation	Activity planning, self-assertiveness training, relaxation techniques, stress management, use of external memory aids, memory training, and motor exercise	group (10)	30 MCI 10 AD	no
Lee (43)	RCT	Computer-assisted errorless learning program	The basic training principles were: the learned task was broken into components; overlearning of components through repetition; training from simple to complex gradation (e.g. two answers upgraded to three answers); immediate positive feedback to reinforce learning; a non-	individual	13 AD	yes

			threatening training atmosphere and giving hints; using vanishing cues and spaced retrieval strategies.			
Loewenstein [44]	RCT	Cognitive Rehabilitation (CR) and Mental Stimulation (MS).	CR training included face–name association tasks, object recall training, functional tasks (e.g. making change, paying bills), orientation to time and place, visuo-motor speed of processing and the use of a memory notebook. MS included computer games.	individual	25 AD	mixed
Luttenberger [45]	RCT	MAKS (motor stimulation)	Motor stimulation, practice in Activities of daily living, cognitive stimulation (K) and Spiritual element.	group	30 mixed, incl. AD	no
Niu [46]	RCT	Cognitive stimulation therapy (CST)	CST based on engaging executive functions and working memory; reality orientation task; (verbal) fluency task; overlapping figure task; photo story learning task.	individual	16 AD	
Olazaran [47]	RCT	Cognitive-motor intervention (CMI) in groups of 7-10 plus psychosocial support.	Reality orientation technique, cognitive exercises, ADL training, psychomotor exercises, workshops.	group	37 mixed MCI and AD	no
Onor [48]		Multimodal intervention and rehabilitation program for AD and caregivers.	Caregivers psychoeducation about dementia; AD patients received rehabilitation based on ROT (reality orientation therapy) including memory training, reminiscence therapy and occupational therapy.	group	8 AD and 8 caregivers	no
Rojas [49]	RCT	Cognitive intervention program	Teaching cognitive strategies, cognitive training and use of external aids.	group	15 MCI	no
Rozzini [50]	RCT	TNP and cholinesterase inhibitors	Multidimensional software (TNP); stimulate different cognitive functions, such as memory, attention, language, abstract reasoning and visuo-spatial abilities.	individual	15 MCI	yes
Spector [51]	RCT	Group Cognitive Stimulation Therapy (CST)	Reality orientation, reminiscence therapy, multisensory stimulation, implicit learning.	group	115 dementia	no
Tadaka [52]	RCT	Reminiscence group program	Computerized cognitive training using TNP, occupation therapy and behavioral training.	group	n=26	no
Talassi [53]	CCS	Cognitive rehabilitation	Computerized cognitive training using TNP, occupation therapy and behavioral training.	individual	30 MCI 24 mild AD	yes
Tarraga [54]	RCT	Interactive Multimedia Internet-based System (IMIS)	IMIS was conducted using Smart brain, an interactive multimedia tool, consisting of 19 separate “tasks” or stimulation exercises across the domains of attention, calculation, gnosis, language, memory and orientation. Includes reinforcement of IADL.	individual	15 suspected mild dementia	yes
Troyer [55]	RCT	Multidisciplinary group-based intervention program	Presentation of information regarding a lifestyle factor (e.g., nutrition) that can affect memory	group	24 MCI	no

			function, focused memory intervention training.			
Wenisch [56]	NRCT	Cognitive stimulation program	Reality orientation techniques, newspaper review (i.e., recall of key events), cognitive exercises (memory, executive function, visuo-spatial abilities) by means of an applied cognitive strategy.	group	12 MCI	no
Yamaguchi, [57]	B/A	Error-less learning based on brain-activating rehabilitation (BAR) using video sport games	Sensor-based video games that utilize psychomotor skills, such as hand-eye coordination, require timing, and necessitate fine three-dimensional control of the limbs in space.	individual	9 dementia	yes

Notes: Empty cells denote insufficient information in the publication. Column 'treatment group' lists sample size and characteristics only for the treatment group. Most intervention studies included a similarly sized control group, hence total sample size was about twice as large. For simplicity and ease of comparison with B/A studies only the intervention group sample sizes are listed here. RCT, randomized controlled trial; NRCT, non-randomized controlled trial; B/A, before and after study; CCS, case control study.

Table 1: Intervention study description.

Inventory of Cognitive Intervention Ingredients

During the scoping exercise it became clear that existing intervention strategies consisted of multiple components. Nevertheless, common individual ingredients of the interventions could be distilled from the screened literature and are as follows:

Educational training

This type of training aims to inform patients about their condition. Specifically, it aims to convey knowledge regarding symptoms, such as onset and duration in specific stages (e.g. memory decline).

Strategies to improve memory functions directly by using compensatory techniques

Memory aids: These include external aids, such as note systems, calendars, note pads, memory books, and other systems or prompts. Patients learn their proper use and application in everyday life.

Reality orientation therapy: Patients are repeatedly presented with information, such as name, date, time, place, weather, and news events. This therapy aids patients to orient themselves in time and space and aims to put events into context.

Internal compensatory strategies: These cognitive tools include memory strategies such as mnemonics and logical location, which help memory recall and retention.

Spaced retrieval: This learning technique is also sometimes referred to as 'expanded retrieval' or 'uniform retrieval'. Essentially, patients are asked to recall material they wish to retain repeatedly with the time intervals between recalls being gradually increased.

Visual imagery: In order to facilitate learning and recall, verbal material is associated with visual information to improve memory.

Method of loci: Patients learn to mentally link an item with a place, to improve their memory. Hence, items to be remembered in this mnemonic system are mentally placed in physical locations. This method is also known as 'memory palace' or 'mind palace technique'.

Chunking: This process involves grouping of information together into a meaningful whole. A chunk is referred to as a collection of

multiple smaller inter-associated units. When retrieved, a chunk acts as a coherent group. For example, it is more difficult to remember individual letters, compared to words that comprise these letters.

Categorization and organization: Patients learn to classify and organize information by categories, such as semantic category or order of importance.

Rehearsal based approach: Patients repeatedly practice recall of information and procedures over time until learned and retained.

Errorless learning: This component refers to a cognitive strategy, rather than a cognitive intervention per se. During errorless learning, incorrect or inappropriate responses are eliminated, ensuring that only correct responses are possible, which is believed to facilitate learning.

Vanishing cues: This technique is a form of errorless learning and refers to the systematic reduction of cue information across trials. On the first trial, sufficient cue information is provided to elicit a successful response, and then cue information is systematically decreased, such as reduction of the intensity at which cues are presented.

Cueing: Cueing strategies may be used to help patients initiate certain actions. Essentially, actions are prompted by a specific phonological, tactile, and/or semantic cue. Cues may also be used by the patient (as well as the care giver) for communication purposes, for example in the form of cue cards.

Strategies to improve other cognitive functions

Mind mapping: The use of diagrams to visually record and group associations around a central issue or idea.

Executive function exercises: Executive function refers to concepts such as inhibition, updating, and switching. Specific cognitive exercises exist that may enhance executive function. As part of executive function exercises 'problem-solving' strategies may be taught. These include various strategies, such as 'divide and conquer', whereby the problem is broken down into multiple smaller and more manageable parts, or 'analogy', which is applying the solution to a similar problem to solve a current problem.

Working memory training: Working memory capacity and efficiency is a key predictor of a wide range of cognitive functions and fluid intelligence. N-back tasks are designed to specifically train working memory functions like set shifting and updating, and have been shown to produce structural changes in relevant brain regions [58], as well as effects on tests of working memory and other cognitive domains [59–61].

Dual-task training: This component, which also uses working memory, comprises ingredients of both, cognitive and physical interventions, hence 'dual-task'. It aims to train motor-cognitive and cognitive-cognitive dual tasks, such as walking while talking or simultaneously performing a summing task and a visual search task [62,63]. In essence, this means that a cognitive intervention ingredient is added to a physical intervention, or two cognitive intervention ingredients are added together and practiced in concert. Theoretically all cognitive intervention ingredients could be combined with a physical intervention or each other; however, some ingredients are better suited, such as cognitive games or executive function training, due to practical issues. This approach is therefore not an ingredient per se, but rather describes a strategy by which certain ingredients can be combined. Nevertheless, performing two tasks simultaneously likely affects additional cognitive domains on top of the domains targeted by the involved intervention ingredients, as managing the two simultaneous tasks requires additional cognitive processes. Dual-task training can therefore also be seen as a cognitive intervention ingredient, aiming to strengthen the simultaneous handling of various multi-domain tasks.

Mental and cognitive exercise: Patients perform mental and cognitive exercise when they engage in mentally stimulating tasks, such as learning or speaking a foreign language, as well as breaking common habits, e.g. taking a different route to work. This may refer to non-specific cognitive engagement as well as engagement in tasks and exercises designed to be mentally stimulating.

Cognitive games: The aim of this ingredient is to stimulate mental activity, including memory, calculations, and perception in a playful manner. This ingredient may include computerized video games for leisure as well as games specifically designed to enhance mental capacity.

Reminiscence therapy: Patients discuss, recall, and share remote events and memories from their past, such as childhood memories or pop cultural events, which is believed to improve cognitive function and mood.

Recreational use of computers and technology: This ingredient refers to the practice of computers and other related devices for recreational or leisurely use, such as surfing the Internet, email programs, apps (e.g. news), and browsers. This ingredient does not include video or computer games.

Dyadic approach: Not all cognitive intervention approaches are directly aimed at patients. The dyadic approach aims to teach caregivers and family members to carry out memory and cognitive improvement strategies. This approach also includes teaching caregivers and family members about diseases, such as dementia, in order to increase their understanding of the condition.

Target cognitive domains and tests

A range of cognitive domains are commonly targeted by cognitive interventions. Some of the ingredients target multiple domains, while

others are more focused. Generally, there is no consensus as to the exact domains affected by specific cognitive training strategies. Most cognitive interventions comprise multiple active ingredients, and as a result the observed effects cannot be unambiguously attributed to a specific intervention ingredient.

The list below is a selection of cognitive domains which are frequently targets of cognitive intervention ingredients. The term 'immediate' indicates that a domain refers to 'short term' or 'working' memory, while the term 'delayed' refers to 'long-term' memory. A further distinction can be made between 'recall' and 'recognition'. 'Recognition' essentially refers to remembering having experienced or encountered something previously, while 'recall' refers to accessing and retrieving a full memory trace located in long-term memory.

Global cognitive functioning: This component refers to the intellectual processes of acquiring and comprehending knowledge and ideas and comprises all aspects thereof, such as perception, reasoning, attention, working memory, problem solving etc. Essentially, global cognitive function is a composite domain of all sub-domains belonging to cognitive function. Example tests include: mini mental state examination (MMSE) [64] and montreal cognitive assessment (MoCA) [65].

Auditory/Verbal memory: This domain refers to memory of words and other concepts involving language. Example tests to assess this domain are: Hopkins Verbal Learning Test (HVLT) [66] and Rey Auditory Verbal Learning Test (RAVLT) [67,68]. Some tests like the HVLT comprise immediate (recall directly after word list presentation) and delayed recall (about 20 minutes after initial word list presentation) measures, where working memory plays a potentially greater role in immediate recall and delayed recall is more related to longer-term learning. These processes are thought to rely on quite different neural substrates, and there are a range of tests that are designed to measure working memory capacity and efficiency more explicitly, e.g. n-back tasks [69] or measures of primacy and recency effect strength, but these are not commonly used in studies of age-related cognitive decline. There is also a difference in recognition and recall outcomes on many word list memory tests. Recognition is easier than full recall, and it may also rely more on extra-hippocampal areas in the medio-temporal lobe, whereas recall is thought to require the hippocampus and pre-frontal areas to a greater extent [70,71].

Visuospatial memory: Spatial memory is an individual's knowledge of the space around them and their relative location in it, as well as memory of and navigation to and from certain locations. Visual memory refers to the encoding, storage and retrieval of shapes and colours. In practice spatial memory ('where') and visual memory ('what') often interact, as part of spatial memory involves visual information and vice versa and is therefore referred to as visuospatial memory. Examples of tests include: Corsi Block Span [72] and Rey-Osterrieth complex figure test [73,74]. Similar to the auditory domain, short or long delays before recall or recognition can be used, which measures of probably distinct underlying neural and cognitive processes.

Verbal fluency (semantic and phonemic): Verbal fluency commonly describes individuals' speed of speech as well as the ability to access mental vocabulary when producing speech. It requires intact verbal memory, executive function (for search and retrieval) and language functions. Semantic and phonemic fluency are the two most common parameters tested. Semantic fluency refers to the capacity to name exemplars of categories (animals or fruits). A phoneme is essentially a

unit of sound that allows distinction between words. Phonemic fluency for example describes the ability to name 4-letter words that begin with the letter 'L'. Both aspects are assessed in the Verbal Fluency Task.

Executive function: Executive function refers to the capacity to inhibit irrelevant information, regularly update information in changing environments, and switch from irrelevant towards relevant information [75]. It comprises concepts such as working memory, cognitive flexibility, multitasking, planning, and attention. This domain includes problem-solving, which refers to the steps individuals use in order to attain a desired outcome. These steps include the recognition and definition of a problem. This is followed by the identification of (multiple) plans for problem resolution and plan selection as well as implementation. Finally, the outcome is evaluated. Problem-solving is a higher-order cognitive process, requiring modulation of several other cognitive skills. Example tests to examine this domain are: Stroop test [76], Trail Making Test (TMT-B) [77], and Tower of London test [78].

Information processing speed (IPS): This domain essentially refers to the pace of individuals' cognitive operations. It has also been described as efficiency of cognitive function and expressed as reaction times, or time taken to complete a task. Example tests are reaction times and symbol digit modalities test (SDMT) [79,80].

Activities of daily living (ADL): ADL are not a purely cognitive domain per se, but require the operation and interaction of multiple cognitive as well as non-cognitive functions. The term generally refers to self-care activities, such as 'preparing food' or 'making a phone call'. Examples of tests include the Bristol ADL scale [81], as well as instrumental ADL (IADL) [82] scale.

Technology Aspects

Most cognitive intervention ingredients are already digitally available or have the potential of being computerized or computer-based. With the advent of sophisticated mobile technologies, such as tablets, smartphones and associated applications as well as sensors, the facility of computerizing traditional cognitive interventions has greatly increased. In fact, numerous studies have attested the efficacy of computer or phone-based cognitive interventions [1]. In particular, their cost-effectiveness renders computer-based cognitive interventions as promising tools against cognitive decline. The regular and leisurely use of computers per se has been linked with a reduction in cognitive decline, for example as shown by the English longitudinal study of aging (ELSA) [83].

Overall, computer-based interventions bear advantages over traditional interventions, such as standardization of administration and stimuli, automatic evaluation of performances and comparison to previous performances, as well as reduced workload for care-givers [84]. At the same time, criticism regarding the increasing computerization of cognitive interventions has been raised, pointing out that elderly individuals are often anxious to use unfamiliar computer or mobile technology [85], although this may be less problematic in the future.

Several software packages for cognitive computer-based interventions already exist, among others neuropsychological training (NPT) [27], Big Brain Academy [30], or 'Cognition 1' [36]. In the light of these developments and given the processing power of current mobile technology, the transition from home computers to mobile technology should be facile and fluent. In fact, leisurely use of the

Internet, email programs, and browsers is already widely-established among smartphone users. In this case, interventions should focus on familiarizing older adults with the relevant technologies.

Educational training also lends itself for being conducted online, via blogs, forums, encyclopaedias, massive open online courses (MOOC), and websites, thereby also stimulating an exchange between individuals. Similarly, forums or comparable online-tools may be used to stimulate individuals to reminisce about the past. Simple programs can be developed, which prompt patients to recall and record past events, by means of video, voice, or text processing. Voice and text recognition programs could analyse the content of recorded footage, ask content-related questions, and prompt further reminiscence, enabling the user to actively interact with the artificial intelligence. The potential for the detection of emotions and computers' responsiveness in this context exists via analysis of tone of voice and facial expressions, but is still in a developmental stage.

Daily use of online sources such as through smartphone apps including news, date, time, place, and weather, can also help individuals' orientation in time and space, greatly facilitating the implementation of reality orientation therapy. Leisure games for smartphones are already widely available (e.g., chess or Sudoku) and are routinely used by smartphone and tablet users. The development and implementation of cognitive games can thus be based on translating existing pen and paper games and home computer games with documented beneficial cognitive effects to mobile technology that can be used by the target populations. In the same way, intervention ingredients aimed at increasing function in other domains, such as executive function, may be implemented for use on smartphones and computer systems.

Many of the existing cognitive intervention ingredients include teaching patients certain skills or strategies. Computer and mobile technology is uniquely suited as an instructional tool. As such, detailed step-by-step directions can be written and/or recorded in the form of instructional videos and workshops. The use of external and internal memory aids, method of loci, or problem-solving skills, can therefore be taught effectively through instructional videos. Furthermore, using video-chat technology experts can be contacted to aid patients with the use of software, and to support longer-term engagement with the cognitive intervention strategy.

Lastly, variation in cognitive function increases with age, and several authors have attributed this to sensorimotor deficits [86]. These can include reduced visual or auditory processing due to cataracts or peripheral deafness, and possibly psychomotor dysfunction related to stroke or other neurological disorders such as Parkinson's disease, and common age-related morbidity, such as arthritis. They can affect how people are able to interact with technological devices and training materials. However, despite these deficits, computerized cognitive training has been shown to be feasible and effective in various pathological conditions such as Parkinson's disease [87] and stroke [88]. Computerized interventions and tests might actually offer optimized and adjustable interfaces to overcome some of these deficits, e.g. by allowing for changes in response button size and sensitivity, and adjustments in font size and background colour and sound volume. For example, our earlier work showed that adjustments need to be made for people with dementia, related to specific vision and possibly gait changes [89,90]. More work should be done to explore and adjust to the specific needs arising from sensorimotor deficits to make best use of the possibilities offered by modern technology.

Suitability for Group-Based and Individual Programs

The utility of group-based approaches and individual or home-based approaches is largely dependent on the specific intervention ingredients employed. In essence, group-based approaches bear the advantage of treating a number of patients at the same time in a social setting; however, this can be seen as a disadvantage as well, as a professional instructing a group of four individuals cannot devote as much time and attention to each individual group member as during a one-on-one session. Therefore, in the case of certain cognitive intervention ingredients group-based approaches may be more time and cost-efficient, as multiple individuals can be treated simultaneously; however, this is not to say that a group approach is necessarily always superior or more efficacious. For example, during reality orientation therapy, news articles, weather, and other issues of interest can be discussed in a group, which means that several patients can be treated at the same time. Exchange among patients is particularly stimulating and beneficial for several cognitive domains.

The group approach may, however, require a certain level of cognitive functioning among patients. In the case of severely demented patients for example, reality orientation has to be more individualized, such going over individuals' names and personal histories, which may be less effective and feasible in a group setting. Similarly, the use of memory aids, external and internal memory strategies, may be most efficiently taught in small groups. Cueing on the other hand, may be difficult to achieve in groups, as it requires specific phonological, tactile, and/or semantic cues, which are often highly individualized.

Computerized intervention ingredients are generally considered to be individual activities. They are, nevertheless, also well-suited for use in small groups. Supervised computer-based interventions, whereby an instructor can provide immediate feedback and aid in task completion, are an example of computer-based intervention strategies used in a group setting. Furthermore, video games designed for leisure as well as cognitive games can possibly be played in small groups on one device or multiple devices via the Internet or local area network, hence in multiplayer mode, which allows the integration of a social component to the cognitive domain. In essence, there are merits to both, individualized and group-based approaches and computer or smartphone-based cognitive intervention ingredients can be used in both instances. Generally, the choice between a group and an individual approach depends on the existing level of cognitive function, the amount of assistance patients require, as well as the available facilities.

Conclusions

The issue of categorization in the context of cognitive intervention strategies has led to some confusion and puzzlement in the scientific community and among care providers. We advocate the abolishment of umbrella categories altogether, as there appears to be no system that adequately represents the manifold cognitive intervention strategies, ingredients, and protocols available. Here we attempted to focus on the identification of more basic ingredients of cognitive interventions, to derive a more systematic and flexible toolbox for building and individualising cognitive interventions. Nevertheless, this list does not aspire to be exhaustive and will of course need to be updated as methods evolve. Furthermore, the literature sample on which these cognitive intervention ingredients are based is small and was not systematically selected. Lastly, there may be overlap between the target domains and respective tests identified in this paper. These limitations

invite prudence and as well as discussion, additions, and adjustments to the proposed intervention ingredients. The listed ingredients are also not necessarily mutually exclusive. For example, reminiscence therapy can be administered in the form of a cognitive game. Furthermore, combinations of ingredients may be more efficacious than individual ingredients per se. In fact, the combination of ingredients might represent an avenue for deriving novel approaches with good efficacy and end user acceptance to enhance long-term engagement. Future reviews should focus on identifying the most optimal combinations of ingredients to promote best outcomes based on cognitive impairment severity. In order to do so, however, it is necessary to examine the efficacy of the individual ingredients first. As there are currently no studies examining the efficacy of intervention ingredients individually, we cannot allocate any of the effects in the respective studies to individual ingredients, which unfortunately also precludes meta-analyses. It may therefore very well be that only a unique combination of certain ingredients is potent enough to actually achieve an effect on a specific domain. It will be essential for future research to test the individual and combined effects of these ingredients, such that we can arrive at a list of effective treatment ingredients. To avoid the same issues surrounding the categorization of cognitive intervention strategies, intervention ingredients should also be standardized in some way. Aside from facilitating comparisons between investigations, clinicians and other providers of care would greatly benefit from well-defined, validated, and replicated intervention ingredients.

The increase in computerization of intervention ingredients is a step towards standardization of care. Computer-based intervention protocols are cost-effective, non-invasive, and easy to implement, with limited demand on human and monetary resources. Furthermore, computer programs should be designed to be self-sufficient. This means that proper use should be clearly described and delineated as part of the program itself, such that reliance on human instructors is minimized. This can be achieved by extensive tutorials, which may form part of the program. A major challenge in the computerized delivery of intervention ingredients will be the acceptance by technology-anxious individuals. However, this may be less of an issue for future generations. In current practice, however, the mere provision of a computer program often does not lead to desired adherence and outcomes, especially amongst elderly users that do not routinely rely on computers and smartphones. Issues that need to be considered further in this context are technology-related motivation and self-efficacy, both of which affect individuals' ability to persist and succeed with interventions, as they are related to facing rather than avoiding challenges. We propose a novel approach to collating evidence based reviews to identify those interventions most likely to lead to beneficial outcomes.

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