The Design, Evaluation and Reporting on Non-Pharmacological, Cognition-Oriented Treatments for Older Adults: Results of a Survey of Experts

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Abstract

Introduction

Cognitive decline and dementia significantly affect independence and quality of life in older adults, therefore, it is critical to identify effective cognitive oriented treatments (COTs) (e.g., cognitive training, rehabilitation) that can help maintain or enhance cognitive functioning in older adults, as well as reduce dementia risk, or alleviate symptoms associated with pathological processes.

Methods

The Cognitive Intervention Design Evaluation and Reporting (CIDER), a working group from the Non-Pharmacological Interventions Professional Interest Area (NPI-PIA) of Alzheimer's Association conducted in 2017 a survey with experts in COTs worldwide. The survey's aims where threefold: 1) determine the common attitudes, beliefs, and practices of experts involved in the COTs research targeting older people; 2) identify areas of relative agreement and disagreement among experts in the field; 3) Offer a critical review of the literature, including recommendations for future research.

Results

The survey identified several areas of agreements among experts on critical features of COTs, and on study design and outcome measures. Nevertheless, there were some areas with relative disagreement. Critically, expert opinions were not always supported by scientific evidence, suggesting that methodologic improvements are needed regarding design, implementation and report of COTs. There was a clear consensus that COTs provide benefits and should be offered to cognitively unimpaired older adults, mild cognitive impairment (MCI), and mild dementia, but opinions differed for moderate and severe dementia. In addition, there is no consensus on the potential role of COTs on dementia prevention, indicating that future research should prioritize this aspect.

Discussion

Evidence of COTs to older adults is encouraging, but additional evidence is needed in order to enhance dementia prevention. A consensus building and guidelines in the field are critical to improve and accelerate the development of high quality evidence of COTs to cognitively unimpaired older adults, and those with MCI and dementia.

Introduction

There is a considerable growth of interest in non-pharmacological interventions for older people due to their potential for reducing dementia risk and alleviating symptoms associated with age-related pathological processes. Cognition-oriented treatments (COTs) represent a group of non-pharmacological intervention approaches that received a great amount of attention from both the public and scientific community, and this is reflected in them being included in the World Health Organization's guidelines for risk reduction of cognitive decline and dementia (WHO, 2019). The term COTs refer to a range of techniques applied to engage cognition with various degrees of breadth and specificity. They aim to improve or maintain cognitive processes, and/or to address the impact of cognitive impairment on functional ability in daily life (Bahar-Fuchs, Martyr, Goh, Sabates, & Clare, 2019). COTs is increasingly being recognized as-beneficial for older people since engaging in cognitively stimulating activities can be a protective for age-related cognitive decline (Rebok et al., 2014) and dementia (Barnes & Yaffe, 2011; Edwards et al., 2017) possibly by increasing cognitive reserve and resilience in later life (Stern, 2013; Stern et al., 2018).

Several terms have been used to refer to the methodologies adopted by COTs, and these include cognitive stimulation, cognitive training, and cognitive rehabilitation. While *cognitive stimulation* involves activities targeting cognitive or social functioning in a non-specific manner; *cognitive training* tends to be more specific and applies or teaches theoretically oriented techniques targeting cognitive processes. *Cognitive rehabilitation* involves programs tailored for individual goals, and is centered on performance of specific activities of daily life (Clare, Woods, Moniz Cook, Orrell, & Spector, 2003). A further distinction described in the literature is between rehearsal-based COT approaches, which emphasize the repetition of information over time, and assumes that cognitive processes will improve through repeated practice, and strategic approaches, which emphasize altering the manner in which information is processes or a task is performed to compensate for cognitive deficits (Belleville, Mellah, de Boysson, Demonet, & Bier, 2014). Strategic approaches can involve the use of *external aids* to facilitate task performance (e.g., using a calendar, grocery list or note system), or of *internal strategies*, reflecting cognitive '*tools*' that facilitate a deeper level of processing, and task performance (e.g., mental imagery, mnemonics to facilitate organization, and association of new information) (Hampstead, Gillis, & Stringer, 2014).

One of the premises of COTs (especially those involving a cognitive training component) is that training or teaching techniques to improve a cognitive ability or process will lead to transfer of gains beyond the immediate context of the intervention. Researchers typically discuss transfer in terms of near vs. far transfer, but the field lack a consensus/precise definition of what “near” and “far” in fact constitute. The inconsistency in the way near and far transfer are conceptualized and operationalized reflect in part a difficulty identifying the most meaningful way to draw boundaries between ‘near’ and ‘far’, which lead to a limited understanding of transfer effects in the COT literature and restricts our ability to compare the conclusions across studies. According to Karbach and Verhaeghen, near transfer is demonstrated by improvement in performance on tasks not explicitly trained, but that measure the same construct as the construct trained, whereas far-transfer is demonstrated by improvement in performance on tasks measuring a different construct than the one trained (Karbach & Verhaeghen, 2014). A further proposed possibility is to distinguish between *content*-based transfer, reflecting transfer of gains from trained tasks to untrained tasks of a similar nature and content, and *context*-based transfer, which reflect transfer to situations different from the training context in content and format, such as everyday activities (Barnett & Ceci, 2002). To date, it appears that for the most part, the literature has mainly referred to transfer in terms of ‘near’ vs ‘far’, even though (Bier, Ouellet, & Belleville, 2018) a major challenge for the field remains the demonstration of transfer of benefits from COTs to different contexts and meaningful activities of daily life.

The body of evidence in relation to COTs across the aging spectrum has been recently summarized in a Systematic Overview (Malmberg-Gavellin et al. 2019 *In Press*). There is evidence to suggest the possible benefits of COTs for global cognition in cognitively unimpaired (CU) older adults (Edwards, Fausto, Tetlow, Corona, & Valdes, 2018; Gates, Rutjes, et al., 2019; Karbach & Verhaeghen, 2014; Lampit, Hallock, & Valenzuela, 2014; Melby-Lervag, Redick, & Hulme, 2016; Mewborn, Lindbergh, & Stephen Miller, 2017; Mowszowski, Lampit, Walton, & Naismith, 2016; Nguyen, Murphy, & Andrews, 2019; Reijnders, van Heugten, & van Boxtel, 2013; Simons et al., 2016) , in those with mild cognitive impairment (MCI) (Belleville et al., 2018; Chandler, Parks, Marsiske, Rotblatt, & Smith, 2016; Hampstead et al., 2014; Hill et al., 2017; Miotto, Batista, Simon, & Hampstead, 2018; Reijnders et al., 2013; Sherman, Mauser, Nuno, & Sherzai, 2017; Simon, Yokomizo, & Bottino, 2012; Zhang et al., 2019), and, to some extent, in people with dementia (PwD) (Bahar-Fuchs, Clare, & Woods, 2013; Bahar-Fuchs, Martyr, et al., 2019; Clare, 2017; Clare et al., 2019; Hill et al., 2017; Hindle et al., 2018; Kallio, Ohman, Kautiainen, Hietanen, & Pitkala, 2017; Voigt-Radloff et al., 2017).

In the context of CU older adults, randomized controlled trials have shown benefits of COTs in cognitive domains that typically decline as a function of age, such as attention and executive control (Anguera et al., 2013; Belleville et al., 2014; Bherer et al., 2008; Bier et al., 2018; Boot et al., 2010; Stern et al., 2011), working memory (Borella, Cantarella, Carretti, De Lucia, & De Beni, 2019; Borella, Carretti, Riboldi, & De Beni, 2010; Brum, Borella, Carretti, & Sanches Yassuda, 2018; Simon, Tusch, et al., 2018), speed of processing (Ball et al., 2002; Smith et al., 2009), episodic memory and reasoning (Ball et al., 2002; Willis & Caskie, 2013). The combination of different domains (i.e., executive processes, working memory, episodic memory and speed) and other modalities of lifestyle intervention (i.e., exercise, nutritional counselling and health management) has also resulted in cognitive gains (Ngandu et al., 2015). In addition, there is evidence that domain-specific cognitive training protocols can lead to cognitive and functional benefits lasting as long as 10-years (Rebok et al., 2014), and may be associated with reduced dementia risk (Edwards et al., 2017). Other studies have shown memory benefits after internal cognitive strategy training (e.g., mnemonics) for CU older people and those with MCI (Balardin et al., 2015; Belleville et al., 2011; Belleville et al., 2018; Hampstead, Sathian, et al., 2012; Hampstead, Stringer, Stilla, Giddens, & Sathian, 2012; Hampstead, Stringer, Stilla, & Sathian, 2019; Simon, Hampstead, et al., 2018; Simon et al., 2019) as well as following external strategy training, such as the use of a calendar or note system (Chandler et al., 2017; Greenaway, Duncan, & Smith, 2013). Cognitive strategy training focused on memory has been the main approach studied in MCI, since memory deficits are prevalent in this population, and despite encouraging results, there are also negative findings in the primary cognitive outcomes (Olchik, Farina, Steibel, Teixeira, & Yassuda, 2013; Vidovich et al., 2015). Beyond cognition, there is some evidence that COTs may lead to gains in quality of life, mood, self-efficacy (Chandler et al., 2019) and metacognition in those with MCI (Bahar-Fuchs et al., 2017; Belleville et al., 2018; Simon, Hampstead, et al., 2018). Considering PwD, a recent systematic review concluded that, relative to a control intervention, cognitive training may be associated with moderate effects on overall cognition, but CT-related cognitive gains were no different than gains associated with alternative structured treatments (Bahar-Fuchs, Martyr, et al., 2019). Data from individual trials suggests that goal-oriented cognitive-rehabilitation may be an effective approach to improve personal satisfaction with the performance of relevant activities of daily living (Bahar-Fuchs et al., 2013; Clare et al., 2019; Hindle et al., 2018; Regan, Wells, Farrow, O'Halloran, & Workman, 2017), and a protocol for a systematic review of the literature in this area has been recently published (Kudlicka et al. 2019).

Despite the encouraging evidence of COT-related benefits in the older population, it is not clear to what extent clinicians and researchers rely on these interventions, and what their opinion is regarding their use. Methodological issues in the design, evaluation and reporting of COT trials continue to challenge researchers and clinicians, leading to difficulty drawing firm and consistent conclusions, and more than likely restricting their implementation in clinical and community settings. These include substantial variability across intervention design and trial-methods, typical small sample sizes and limited statistical power which lead to inconsistencies across studies. In addition, intervention protocols vary in terms of the cognitive process targeted, the approach utilized (e.g., rehearsal or strategy-based), as well as such factors as the setting, format, level of supervision, frequency, dose, type of control condition (if any), outcome measures, follow-up period (if any), and statistical methods used. In particular, the rationale behind many methodological decisions is often unclear and/or unspecific, and testable hypotheses are not always provided.

Against this background, we created the Cognitive Intervention Design Evaluation and Reporting (CIDER) group in 2014 (Bahar-Fuchs, Hampstead, Belleville, & Dwolatzky, 2016; Bahar-Fuchs, Hampstead, & Clare, 2014). The CIDER group is an international expert working party which aims to advance methodological rigor in COT trials, encourage greater consensus and collaboration in the field, and promote more responsible dissemination of research evidence. The group comprises academics and clinicians involved in the research and delivery of COTs to older adults. CIDER is committed to the advancing evidence-based research and practice in this area (including by establishing a novel evidence synthesis platform www.cogtale.org (Bahar-Fuchs, 2018), and to this end are working on the development of research guidelines, and possibly, future consumer guidelines. In 2017, CIDER conducted a survey of experts (researchers and clinicians) to gain insight as to their attitudes, beliefs and practices in relation to several topics involving COTs to older adults (specific details are outlined below). The goal of the survey was to identify areas of relative agreement and disagreement, and to clarify beliefs and gaps in knowledge of experts regarding the design and implementation of COTs. The findings of this survey would potentially form the basis for ongoing expert consensus building activity, while keeping in mind that COT related research and practice around the world is likely to reflect beliefs and values in addition to scientific evidence. It should be a priority to identify relevant factors that influence COTs research in order to improve the design, implementation and reporting of study methods. Greater consensus among researchers and clinicians is certainly likely to improve and accelerate the development of evidence-based practice.

The present study

The present report details the results of the survey of experts. The primary aim of the survey was to determine the common attitudes, beliefs, and practices of researchers involved in the design and conduct of COTs studies targeting older people. A second aim was to identify areas of relative agreement and disagreement among experienced researchers and clinicians involved in COTs research and implementation. A third aim was to offer a critical review of the literature and propose recommendations for research methodology based on the survey responses. It was anticipated that the survey would reveal gaps in knowledge and beliefs of experts regarding the design and implementation of cognitive intervention studies, including aspects such as characteristics of COTs.

Method

Survey

The survey was developed in an iterative fashion by collaboration between CIDER members in early 2017 and was designed to take approximately 30 minutes to compete. It aimed to investigate the knowledge, common beliefs, and attitudes regarding COTs held by researchers and clinicians working with older people. The survey was divided into eight sections, as presented in Table 1.

[Table 1]

Participants

Potential participants were recruited via the Non-Pharmacological Interventions Professional Interest Area (NPI-PIA) of Alzheimer's Association ISTAART (International Society to Advance Alzheimer's Research and Treatment) network, of which CIDER is a working party, as well as by directly contacting the first and last author of COT trials published in recent years. The survey was sent to 120 academic and/or clinical researchers with expertise in the design and delivery of cognition-focused interventions for older adults. The experts' work was focused on at least one of three target populations: 1) healthy older adults (e.g., CU), 2) older adults at significant risk for dementia (e.g., MCI), or 3) adults living with dementia (e.g., verified dementia diagnosis).

Procedure

Preliminary concepts and ideas for the survey were discussed during regular monthly CIDER meetings in 2016, and the survey was drafted in an iterative fashion in early 2017. The project was reviewed and approved as a Negligible Risk Research Project by the Melbourne Health Human Ethics Review Committee (Melbourne, Australia, approval number QA2017037). The survey was developed and disseminated using the Qualtrics online survey tool (Qualtrics, Provo, UT), and was available from May to June 2017. In addition to being sent directly to specific researchers based on their scholarly output, the survey was further promoted via the international NPI-PIA network, and the Alzheimer's Association ISTAART newsletter. Participant information was provided in a preamble at the start of the online survey. Respondents were then asked to give consent in order to access the survey, which could be discontinued at any time by the respondent closing their browser.

Consensus Meeting and Discussion

After the survey was completed, the CIDER committee organized the presentation of the survey results at a consensus-building meeting at the Alzheimer's Association International Conference (AAIC) in London, UK during July 2017. The meeting included nine leading authors in the field from different countries (i.e., Australia, Canada, China, Israel, United Kingdom, and United States). The participants were encouraged to actively discuss the survey topics, provide their opinions and raise relevant hypotheses. The objective of this meeting was to present and discuss the survey results, and the level of agreement on the effectiveness of COTs for older adults who were cognitively unimpaired (CU), or were determined to have MCI or dementia.

Data Analysis

The data were analysed by quantifying frequencies associated with different response options to the various survey questions. Responses are reported in terms of the level of agreement with Likert scales, ranking of items from high to low, and the frequency of selected options from a list. Quantities are reported as percentages, with 100% representing all completed survey responses recorded.

Results

Respondent characteristics

Of the experts invited by email, 39 (32%) commenced and 32 (26.5%, 50% women) completed the survey, with respondents from 15 countries (Figure 1). Ages range varied from 25 to 75 years, and 81% had over ten years of experience working in medical (25%), psychological (75%), academic (60%) or combined clinical and research (40%) settings. All respondents reported involvement with implementation of cognitive interventions, and 22% were able to prescribe medications. Approximately one third of the respondents had expertise in COTs with MCI (33%), followed by mild-to-moderate dementia (25%), CU (23%), moderate-to-severe dementia (8%), and other populations (e.g., Parkinson disease, late-life depression, subjective cognitive decline, semantic dementia). Regarding intervention type, 41% of the respondents reported expertise in cognitive training, 21% in a mix of methods, 15% in strategy-oriented techniques, 12% in cognitive stimulation, 3% in cognitive rehabilitation and 3 % in education programs. For illustration of experts characteristics, see Figure 1S (Supplemental Material).

[Figure 1]

COTs critical features

Respondents were asked to indicate their opinion regarding the relevance of several intervention components and classify them as: 1) "Critical", meaning that the treatment is very unlikely to be effective without this component; 2) "Optimal", meaning that the treatment may be improved by the inclusion of this component, but the success does not depend on it; and 3) "Irrelevant", meaning that the treatment feature is unlikely to be associated with any benefits.

COTs features are summarized in Figure 2. There was relative consensus among the respondents on the features deemed *critical* to the effectiveness of COTs, since more than 50% of the responders considered the following features as "critical": 1) tasks or activities should be adaptive; 2) barriers to performance and adherence should be identified; 3) problem solving should be provided for barriers to performance and adherence; 4) practical and 5) emotional support should be available to participants; 6) goals should be evaluated and revised as appropriate; 7) repeated practice; 8) specific instruction on intervention methods should be provided; 9) direct coaching or instructions; 10) feedback on performance; and 11) focus on relative weaknesses. There was also relative agreement that certain intervention features should be considered or incorporated optionally in COT trials, including 1) focusing on relative strengths of the participants; 2) psychoeducation; 3) remote performance monitoring; and 4) ensuring the participant regards therapist as an authority. Finally, there was relatively low consensus regarding the importance of some intervention features, such as: 1) monitoring performance with participants; 2) goal setting by the participant; and 3) setting pre-determined intervention goals.

[Figure 2]

COTs approaches & targets

The majority of respondents (80%) agreed that the distinction between COTs approaches typically described in the literature (e.g., cognitive stimulation, cognitive training and rehabilitation) reflect important differences in treatment and mechanisms of action. For example, 70.5% of respondents considered individualized goal setting (GS) as an essential component of the cognitive rehabilitation approach only, but not for cognitive training (14.7%), strategy training (8.8%) and cognitive stimulation (5.8%). In relation to the populations being targeted by a particular type of intervention, there was relative agreement that COTs should not target a single cognitive domain, particularly for individuals with mild-moderate dementia (80% agreement), but also for older adults with MCI and CU (68.5% and 65.7% of agreement, respectively) (see Figure 3A). According to most–respondents, COTs should focus on impaired or weaker cognitive functions (i.e. cognitive weakness) rather than intact cognitive functions (i.e., relative cognitive strength) particularly in those with MCI (72.7%) and dementia (66.6%), but this was not deemed as important in CU older adults (39.3%). It was agreed that cognitive strategies were more relevant to outcomes for CU older adults (63.6%) and those with MCI (60.6%), but not so useful for PwD (45.4%) (Figure 3C). Regardless of the intervention approach or the targeted cognitive domains, 67.6% of the respondents agreed that cognitive strategy training is the primary mechanism of action required to support transfer of gains from trained to untrained tasks. Regarding focus of the intervention (Figure 3D), most of the respondents believed that both structured cognitive tasks and daily activities should be targeted in COTs for CU adults (60% agreement), and MCI (80%). However, for PwD, the focus of the intervention considered optimal was daily activities only (62%).

[Figure 3]

COT's design & outcome measures

The design characteristics of COTs were analyzed considering five categories: format of intervention (e.g., individual or group delivery), setting (e.g., clinic or community location), level of supervision (e.g., remote or face to face), the dose (e.g., total number of sessions), and frequency (e.g., how many sessions per week or month) (Figure 4). Regarding the intervention format (Figure 4A), the preferred format for both CU older adults and MCI was *small group* (39.3%, and 42.2%, respectively); and for those with mild to moderate dementia was *one on one* (36.3%). In addition, respondents agreed that *moderate-large group* is not optimal for those with MCI or dementia, nor a 'one on one' format for CU older adults. When asked to rank the optimal setting for COTs (Figure 4B), the dominant view concerning people with MCI and dementia was the *combination of home, community, and clinic*, while respondents most commonly stated that the setting '*doesn't matter*' in relation to CU older people. In relation to level of supervision (Figure 4C), for CU people there was relative agreement (63.6%) that *limited remote supervision* (as required or at irregular intervals) would be optimal, while for MCI and dementia *face-to-face supervision by a clinician* would be more appropriate (84% of agreement for MCI, and 97% for dementia). Nevertheless, for MCI *face-to-face supervision* could be *limited* or *regular*, while it should be mostly *regular* in the context of dementia. Regarding dose (Figure 4D), respondents were asked to rank in order of usefulness different dose measurement approaches when designing a treatment trial. The main approaches were *number of sessions per week* and *total amount of time*. Specifically, 42.3% considered *number of sessions per week* the most useful dose criterion, and 73% ranked it as the first or second most useful classification, while 26.9% believed that *total amount of time* was the more relevant dose classification, and 58% ranked it as first or second most useful criterion.

The respondents were asked to choose the minimum frequency deemed to confer cognitive or functional benefits within different populations (Figure 4E). For CU older adults, a marginal majority of respondents (51.5%) considered the minimum COTs frequency to be 1-2 times per week, however 27.2% considered the minimum frequency to be 3-4 times per week, and 15.1% reported 1-2 times per fortnight to be the minimum frequency. For people with MCI, respondents were divided; 48.4% considered 3-4 times per week as the minimum frequency, while 45.4% considered 1-2 times per week. Regarding PwD, opinions were also divided, 39.3% of the respondents considered a minimum frequency of 3-4 times per week, 30.3% considered 1-2 times per week, and 24.2% reported that COTs should be delivered daily.

Participants were asked to rate methods of evaluation of cognitive outcomes in COTs targeting people with MCI (Figure 5A), while considering issues of time, resources, and participant burden. The main evaluation methods considered appropriate were 'informant-reported measure of everyday cognition' (96.8% agreement) and 'abbreviated cognitive battery' (90.6%), followed by 'interview-based functional cognitive evaluation' (87.5%), 'self-measure of everyday cognition' (81.2%), and 'full length / comprehensive cognitive battery' (65.6%). The evaluation methods with more disagreement was self- administered computerized cognitive battery' (53.1%), and screening battery (global cognition) (46.8%). Moreover, respondents ranked the three most relevant outcomes among a list of 12 outcomes, regardless the population (Figure 5B). The COTs outcomes ranked as 1st in term of relevance were 'domain specific cognition' (56.2%), 'self-reported attainment of functional goals' (50%), and 'global cognitive performance' (45.4%). The outcomes ranked as 2nd most important were 'mood' (66.5%), 'self-reported everyday cognition' (57.1%), 'observed functional performance' (55.5%), and 'self-reported functional ability' (50%). Last, ranked as 3rd most important outcome were 'self-reported strategy use in everyday life' (80%), 'biomarkers' (e.g., brain measures) (66.6%), 'well-being and quality of life' (57.8%), and 'clinical progression' (42.8%).

[Figure 5]

Population benefit, prescription and dementia prevention

According to respondents, the population most likely to benefit from COTs is people with MCI (95%), followed by CU older people (69%), and finally people with mild dementia (30%). People with moderate (6%) and severe (0%) dementia were not considered likely to benefit from COTs. In addition, respondents selected different intervention approaches as more useful to specific target groups (Figure 6). For CU older adults, cognitive training was considered the most relevant approach, while for people with MCI both training and rehabilitation were considered equally useful. For people with mild-to-moderate dementia, cognitive stimulation and rehabilitation were considered the best approaches. For severe dementia, respondents preferred either cognitive stimulation or no intervention in equal proportion, indicating a lack of consensus in this area.

Regarding maintenance of benefits (Figure 7), most respondents believed that for both CU older adults (81.8%) and people with MCI (66.6%), some gains would be retained in the long term (i.e., over a year), but others are likely to wane in the short term (weeks to 3-6 weeks). For PwD, 45% of respondents considered that all gains are likely to be completely or partially lost in the short term and that functioning is likely to return to baseline levels; and 36% considered that gains would completely be lost in the short term and functioning is likely to deteriorate relative to the beginning of the intervention.

In addition, respondents were asked to consider the level of evidence in order to be convinced of the *general usefulness*, *relative* and *absolute effectiveness* of COTs (Figure 8). There was less agreement among respondents regarding the level of evidence necessary for absolute effectiveness than for general usefulness and relative effectiveness of COTs. Briefly, for general usefulness of COTs, the main criteria deemed was *Greater improvement relative to a treatment as usual / waitlist comparison group*. For relative effectiveness, the main choice was *Greater improvement relative to a placebo or active comparison group receiving a treatment similar in all but the active ingredients*. And regarding the absolute effectiveness, the main choice was *Greater improvement relative to both a treatment as usual / waitlist control group and an active or placebo condition but not relative to another treatment known to be effective*.

Finally, we observed a clear agreement among respondents that COTs should be offered to CU older adults (with and without risk of dementia), MCI, and mild dementia, and not much for those with moderate and severe dementia (Figure 9). In terms of prescription of COTs, most responders (56.2%) believed that *evidence of some usefulness in relation to cognitive functioning and/or a clinically meaningful outcome* is enough to recommend COTs, while 25% believe that is necessary to establish *absolute efficacy* in order to prescribe COTs. Finally, 50% of respondents believed that there is enough evidence that COTs can prevent dementia, indicating a lack of consensus for the roles of COTs in dementia prevention.

[Figures 6 - 9]

Discussion

The current study summarized the beliefs, knowledge and practices of 39 experts in the field of COTs in older adults who responded to our survey invitation. We identified several areas of relative agreement among respondents, as well as some areas of relative disagreement, and these are briefly summarized and discussed below.

Key intervention features

There was relative consensus on the general features essential for COTs success, including that 1) the intervention need to be adaptive in difficulty; 2) Participants need to be given the opportunity to *identify* and *resolve* barriers to *adherence* and *performance*; 3) and given *practical* and *emotional support*. Nevertheless, these key ingredients are not always formally incorporated, examined/monitored or reported. For instance, a metanalysis identified that few COT studies reported measurements of adherence (Sherman et al., 2017), and there is evidence that unsupervised interventions (i.e., with less support) are less effective than supervised ones (Lampit et al., 2014). In addition, an adaptive nature of COTs and tailoring to the needs of an individual may play a major role in motivation, adherence and clinical significance of the results. Although adaptive computerized COTs has been shown additional benefits than no-adaptive control protocols (Bahar-Fuchs et al., 2017; Brehmer, Westerberg, & Backman, 2012; Simon, Tusch, et al., 2018; Smith et al., 2009), this is not always observed (Bahar-Fuchs, Barendse, et al., 2019; Flak et al., 2019), indicating the need of further research on this matter. For research into COTs to advance, it is not only essential that key common ingredients are routinely incorporated into interventions, but also that these components, including their dosing parameters are clearly and accurately described in treatment protocols.

Approaches

In keeping with proposed classifications (Bahar-Fuchs, Martyr, et al., 2019; Clare et al., 2003; Hampstead et al., 2014), there was a consensus that the main terms used to describe COTs (i.e., *cognitive stimulation, training and rehabilitation*) indeed reflect different treatment approaches with distinct mechanisms of action. Importantly, although emerging evidence from the neuroimaging literature points to distinct neural signatures underlying strategy based and rehearsal-based COTs (Miotto et al., 2018), the evidence to date is insufficient to clearly differentiate the broad approaches described in the literature in terms of underlying neurobiology.

Targets

We found relative consensus that COTs should target multiple cognitive and non-cognitive outcomes. This belief is not in line with the evidence that single-domain COT interventions are also associated with benefits. For instance, benefits are reported in COTs focused in WM or executive control for CU older adults (Anguera et al., 2013; Belleville et al., 2014; Borella et al., 2010; Brum et al., 2018; Dahlin, Neely, Larsson, Backman, & Nyberg, 2008; Simon, Tusch, et al., 2018; Stern et al., 2011; Weng et al., 2019), and in episodic memory for amnestic MCI (Hampstead, Sathian, et al., 2012; Hampstead, Stringer, et al., 2012; Simon, Hampstead, et al., 2018). Likewise, a metanalysis on COTs in MCI found a significant overall effect for intervention content, indicating that memory focused intervention was more effective than multidomain approach, although the later also showed a significant effect on cognitive performance (Sherman et al., 2017).

We found relative agreement that COTs should target impaired or weak cognitive functions rather than intact cognitive functions in MCI and dementia. COTs targeting cognitive weakness are frequently observed in people with MCI (e.g., episodic memory), which show an improvement in memory performance following COTs (Belleville et al., 2018; Hampstead et al., 2014; Hill et al., 2017; Sherman et al., 2017; Simon, Hampstead, et al., 2018). Studies of multi-domain cognitive training, and in which both intact and impaired cognitive domains are likely to receive some training, have also been associated with cognitive benefits (Bahar-Fuchs et al., 2017; Hill et al., 2017; Sherman et al., 2017). Conversely, PwD may show more limited cognitive improvements following COTs (Bahar-Fuchs et al., 2013; Bahar-Fuchs, Martyr, et al., 2019; Hill et al., 2017), possibly due to more severe impairments in multiple cognitive domains. Hence, for PwD (and to a lesser extent, those with MCI) to benefit from a COT, and particularly to improve new learning, it may be essential to make use of relatively preserved skills and abilities, such as procedural learning (Thivierge, Jean, & Simard, 2014; Voigt-Radloff et al., 2017). For instance, the errorless learning technique can optimize learning by using feed-forward instructions in order to prevent people from making mistakes during the learning process (Voigt-Radloff et al., 2017). Likewise, goal-oriented rehabilitation approach also builds on relatively preserved skills in order to facilitate learning and this approach has shown benefits in terms of everyday functioning (Clare et al., 2019).

Strategies & Techniques

Experts seem to agree that cognitive strategies should be incorporated into COTs when the target population is CU and MCI, but no consensus was found concerning people with dementia. This is in line with work showing that mnemonic strategies can improve cognitive performance in CU or MCI population, such as method of loci (Belleville et al., 2011; Belleville et al., 2018; Belleville et al., 2014), story making, semantic association or clustering (Balardin et al., 2015; Belleville et al., 2018), PQRST (Belleville et al., 2011; Belleville et al., 2018), calendar/notes system (Greenaway et al., 2013), visual imagery (Belleville et al., 2011; Belleville et al., 2018; Giuli, Papa, Lattanzio, & Postacchini, 2016; Jeong et al., 2016), which has been also integrated into associative memory training for face-name (Hampstead, Sathian, Moore, Nalisnick, & Stringer, 2008; Simon, Hampstead, et al., 2018) and object-location (Hampstead, Sathian, et al., 2012; Hampstead et al., 2019). Nevertheless, some techniques that facilitate implicit learning and skill acquisition have shown to be beneficial to individuals with more pronounced cognitive deficits (i.e., MCI and dementia), such errorless learning (Akhtar, Moulin, & Bowie, 2006; Jeong et al., 2016; Kessels & de Haan, 2003; Voigt-Radloff et al., 2017), spaced retrieval (Creighton, van der Ploeg, & O'Connor, 2013; Jeong et al., 2016; Thivierge et al., 2014) and vanishing cues (Haslam, Moss, & Hodder, 2010; Kessels & de Haan, 2003).

COT's design: format, setting, dose and frequency

In terms of intervention format, there was an agreement that small group may be the optimal preference for CU and MCI. This belief likely reflects the view that social engagement is beneficial and therefore should be incorporated in COTs, in line with the evidence that social relations are protective for age-related cognitive decline (Holtzman et al., 2004; Sharifian, Manly, Brickman, & Zahodne, 2019; Zahodne, Ajrouch, Sharifian, & Antonucci, 2019). In addition, it is likely that including the social component in COTs plays a role in motivation and adherence, and may also be more cost-beneficial than an individual approach. Nevertheless, the individual format may facilitate the use of some technologies (e.g., *apps* and virtual reality), and adapt the training difficulty, which has shown to be beneficial (Bahar-Fuchs et al., 2017; Brehmer et al., 2012; Simon, Tusch, et al., 2018). More efforts should be done to incorporate both formats in the same protocol (Ngandu et al., 2015), which may result in additional benefits. For PwD, a relative consensus indicated a preference for a *one-on-one approach*, which allows tailoring of the intervention to the needs/goals of the individual, facilitates learning, and collaboration between the therapist, patient and family/caregiver, consistent with the evidence from the goal-oriented cognitive rehabilitation approach (Bahar-Fuchs et al., 2013; Clare et al., 2019).

Experts regarded the *combination of home, and community or clinic* as the optimal setting for interventions for people with MCI and dementia, although the literature focuses on one or other setting for the most part. In the case of people with MCI, there are several protocols delivered at home (e.g., Bahar-Fuchs et al., 2017; for reviews, see Hills et al., 2016; Gates, Vernooij et al., 2019), or at clinic (for reviews see Sherman et al., 2017; Hampstead et al., 2014), and an increasing number of studies combining clinic setting with home or structured homework (Belleville et al., 2018; Chandler et al., 2019; Greenaway et al., 2013; Jeong et al., 2016; Ngandu et al., 2015). For PwD, there are several cognitive training protocols delivered in the community or residential care settings that have shown small to moderate effects when compared to a control condition, but no effects were found when compared with an alternative treatment (Bahar-Fuchs, Martyr, et al., 2019). In addition, goal-oriented cognitive rehabilitation tends to combine different settings when emphasizing the collaboration between therapist, patient and family or caregiver, and this has been shown to be of benefit (Clare et al., 2019). Whether there are additional benefits from combining settings, and what is the optimal way to achieve this remains unclear. Regarding normal aging, it appears that experts believed that the COTs setting *does not matter*. Although this perception seems in line with the growing body of literature of home-based computerized protocols for CU older adults (Gates, Rutjes, et al., 2019; Karbach & Verhaeghen, 2014; Lampit et al., 2014), contradicts the evidence that home-based COTs are less effective than clinical-based ones (Lampit et al., 2014). Despite that, home-based COTs tend to be more cost-effective in comparison to therapist-led, and have the potential advantage of being adaptive and scalable, allowing access to those who may be frail, have mobility limitations (Kueider, Parisi, Gross, & Rebok, 2012; Lampit et al., 2014) or reside in rural regions.

One of the great challenges is how *dose* is defined and measured in COTs. Dose can be broadly defined as the quantity of a therapeutic agent to be taken in order to achieve a specific effect. In the context of COTs, dose would refer to the exposure necessary to different factors, such as practice a determined cognitive process, or to learn to use a strategy and an information (Hampstead et al., 2014). In the survey, most experts stated that *number of sessions per week* was the optimal way to define and measure dose in COTs, followed by *total amount of (training) time*. Although these dosing parameters are in wide use in COT protocols, they may not provide specific information on dose-response relationships, since they do not directly show how much practice a participant *actually received* in a determined cognitive process or in learning a strategy. Specifically, the contents of a session can vary dramatically across participants even when a manualized intervention is used given the myriad of participant-specific factors that can affect progress (e.g., perseveration, set loss, inattention, fatigue). It is important that future studies attempt to provide more accurate information in relation to this matter, for instance using a *trial based approach* (Hampstead et al., 2014), or *gains per session*. It is worth noting that meta analytic studies did not find an effect of total intervention duration on COTs efficacy (Lampit et al., 2014; Mewborn et al., 2017), although qualitatively interventions that lasted 20 hours or more had larger effects than those that lasted less than 20 hours (Mewborn et al., 2017).

Regarding frequency, there was an agreement that 1-2 times a week is optimal for CU, as reported previously (Balardin et al., 2015; Ball et al., 2002; Belleville et al., 2011; Belleville et al., 2018; Hampstead, Sathian, et al., 2012; Hampstead et al., 2019; Rebok et al., 2014). In addition, two metanalysis found that fewer weekly sessions (e.g. 1-2 or 1-3 sessions) may be more effective than 4-5 sessions (Lampit et al., 2014; Mewborn et al., 2017). Nonetheless, evidence from individual studies shows that COTs delivered 3 times or more per week are associated with cognitive benefits (Borella et al., 2010; Brehmer et al., 2012; Brum et al., 2018; Ngandu et al., 2015; Simon, Tusch, et al., 2018; Smith et al., 2009; Stern et al., 2011). Concerning people with MCI, there was relative disagreement regarding the optimal treatment frequency, which may reflect that benefits are described in COTs incorporating sessions 1-2 times a week (for a review see Sherman et al., 2017; and for more recent reports see Belleville et al., 2018; Simon et al. 2018, 2019; Hampstead et al., 2019), but also 3-5 sessions per week (Bahar-Fuchs et al., 2017; Chandler et al., 2019; Lam, Chan, Leung, Fung, & Leung, 2015; Vermeij, Claassen, Dautzenberg, & Kessels, 2016).

Outcomes and measures

We observed a clear consensus that COTs for MCI should incorporate the measurement of subjective everyday/functional cognitive outcomes (informant or self-reported). Nevertheless, studies do not routinely incorporate these types of measures, which may be important for evaluating transfer effects in daily activities. For instance, an RCT focused on the implementation of the use of calendar/notebook system found an improvement on activities of daily living measured by an informant-based questionnaire (Greenaway et al., 2013). Likewise, functional status improved after a cognitive strategy training in measures assessing medication management and bill paying (Schmitter-Edgecombe & Dyck, 2014), and after strategy training in combination with education on lifestyle and psychosocial support (Giuli, Papa, et al., 2016). Other RCTs that have focused on MST found increase in a self-report measure of strategy use (Belleville et al., 2018), reduction of cognitive complaints (Belleville et al., 2018; Giuli, Fabbietti, et al., 2016), and frequency of memory mistakes in everyday life (Rapp, Brenes, & Marsh, 2002; Simon, Hampstead, et al., 2018). It is relevant to highlight that other COTs found benefits on cognitive performance but no changes in self-report everyday life activities (e.g., Bahar-Fuchs et al., 2017; Jeong et al., 2016).

There was an agreement that both structured cognitive tasks and daily activities should be targeted in COTs for CU and MCI. However, structured cognitive tasks are more frequently incorporated in COTs for these populations (for reviews see Sherman et al., 2017; Hill et al., 2016; Hampstead et al., 2014; Gates et al., 2019, 2019; Lampit et al., 2014; Zhang et al., 2019; Mewborn et al., 2017). Despite that, COTs targeting everyday life have been developed specifically for MCI (Chandler et al., 2019; Chandler et al., 2016). In addition, efforts have been done to develop cognitive tasks that reflect real-life difficulties, such as forgetting people's names or location of objects (Belleville et al., 2018; Hampstead et al., 2008; Hampstead, Sathian, et al., 2012; Simon, Hampstead, et al., 2018), using a note system (Greenaway et al., 2013), or creating virtual reality environment simulating a real-life situation (e.g., supermarket) (Doniger et al., 2018; Ouellet, Boller, Corriveau-Lecavalier, Cloutier, & Belleville, 2018). Future studies should better combine these cognitive tasks and daily activities in order to enhance transfer effects to meaningful real-life situations.

Transfer

Most responders believed that training cognitive strategies is critical to induce transfer of gains from trained to untrained tasks. Although strategy training protocols showed transfer effects from trained to untrained tasks (Belleville et al., 2011; Belleville et al., 2018; Hampstead, Sathian, et al., 2012; Hampstead et al., 2019; Simon, Hampstead, et al., 2018; Simon et al., 2019) this is not consistent (Olchik et al., 2013; Vidovich et al., 2015). Likewise, some transfer effects have been shown in rehearsal approaches as well (Bier et al., 2018; Gates, Rutjes, et al., 2019; Karbach & Verhaeghen, 2014; Lampit et al., 2014; Mewborn et al., 2017; Sherman et al., 2017), therefore transfer effects are not exclusive from COTs focused on strategy training. It is hypothesized that when an individual acquires a new strategy to learn an information, or to complete a task, it is likely to use it in different situations, enhancing transfer to different contexts. Although this seems a critical mechanism, there is not enough evidence that this is the main factor to contribute to transfer. Other factors such as dose may play a relevant role as well, as shown in dose-response studies (Brum et al., 2018; Stepankova et al., 2014). In addition, ecological training protocols and outcome measures may enhance transfer by creating a more daily-life environment. It is critical that future studies address specific factors that contribute to context and content transfer.

Population benefit, prescription and dementia prevention

There was relative agreement that people with MCI are more likely to benefit from COTs than CU, which may reflect a perception that improving cognition and function in clinical populations is particularly meaningful. This assumption is, however, not always supported by empirical evidence from studies that directly compared these populations. For instance, two studies did not find evidence that MCI or CU benefit differently from MST (Belleville et al., 2011; Hampstead, Sathian, et al., 2012). In contrast, others found that people with MCI improved more than CU following training of speed of information processing (Valdes, O'Connor, & Edwards, 2012) and MST (Olchik et al., 2013), and conversely, that CU presented greater improvement after WM training (Vermeij et al., 2016). In addition, there is evidence that CU with better cognitive baseline would present larger training effects (Willis & Caskie, 2013). Despite these findings, a metanalysis on COTs comparing different population did not find that MCI or CU individuals would benefit differently from COTs (Mewborn et al., 2017). Although it is to be expected that CU individuals would outperform people with MCI at both baseline and post-intervention assessments, whether one group shows greater improvement following training relative to the other remains unclear. Regarding PwD, the survey indicated a clear consensus that PwD benefit less from COTs than people with MCI or CU, in line with the frequent negative or limited findings despite some cognitive benefits (Bahar-Fuchs et al., 2013; Bahar-Fuchs, Martyr, et al., 2019; Hill et al., 2017) and functional improvements (Clare et al., 2019; Hindle et al., 2018).

In terms of maintenance of training effects, experts agreed that both CU older adults and MCI might retain COT-related gains in the long run (i.e., over a year), although some benefits are likely to wane in the short term (weeks to 3-6 weeks). This perception is consistent with the evidence from ACTIVE, the cognitive training trial with the longest follow-up period to date, which showed that COTs can attenuate cognitive and functional decline after 10 years (Rebok et al., 2014), as well as reduce dementia risk (Edwards et al., 2017). However, long-term benefits from COTs in people with MCI is not frequently investigated and evidence beyond 1-2 years is limited (Vidovich et al., 2015). Nonetheless, there is consistent evidence that part of the benefits persist following relatively short term delays (i.e., 1 to 6 months) (Bahar-Fuchs et al., 2017; Belleville et al., 2018; Hampstead et al., 2008; Hampstead, Sathian, et al., 2012; Simon, Hampstead, et al., 2018). A critical aspect for future studies using long-term follow-up (e.g., more than one year) is how to interpret long-term benefits considering that individuals with MCI often present with an underlying neurodegenerative disease and are therefore expected to deteriorate. Although there are encouraging data on cognitive benefits of COTs to older adults, there is little evidence (except for ACTIVE trail) on the effect of COTs on dementia risk (Edwards et al., 2017). In order to understand the role of COTs on dementia prevention, future studies should provide more data on long-term outcomes of COTs, such as incidence of dementia.

In conclusion, despite the heterogeneity in COTs and methodological limitations in the field, there are clearly several areas of agreements among clinical and research experts on critical features of COTs, and on study design and outcome measures. Nevertheless, expert opinions are not always supported by incontestable scientific evidence, suggesting that methodologic improvements are needed to provide high quality evidence, and to design, implement and report COTs. These improvements may be facilitated by future development of guidelines for COTs research. There is a clear consensus that COTs provide benefits and should be offered to CU older adults (with or without risk factors for dementia), MCI, and mild dementia, but opinions differ for moderate and severe dementia. Despite the encouraging benefits of COTs for older adults, there is still no consensus on the potential role these treatments could play in relation to dementia prevention, indicating that future research should prioritize this aspect in order to better recommend COTs and potentially enhance dementia prevention worldwide.

Acknowledgments

We would like to thank all researchers and/or clinicians that contributed to the survey, and those who attended the CIDER meeting at AAIC on 2017 in London: Amit Lampit, Glenn Smith, Joshua Scott, Aleksandra Kudlicka and Yi Tang.

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Figure Legend

Figure 1. Countries of Survey Experts

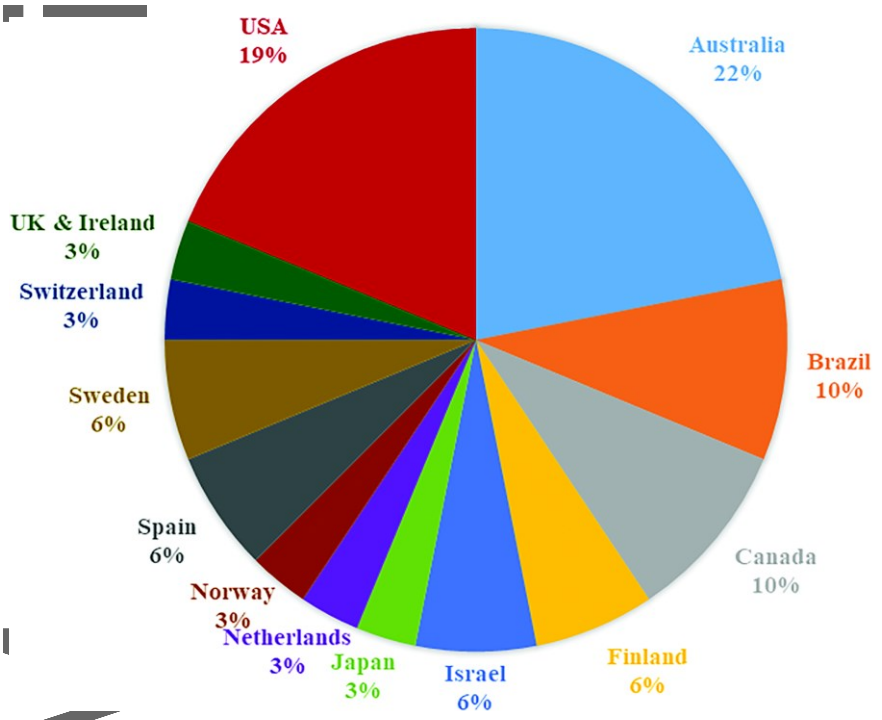


Figure 2. COTs Treatment Features

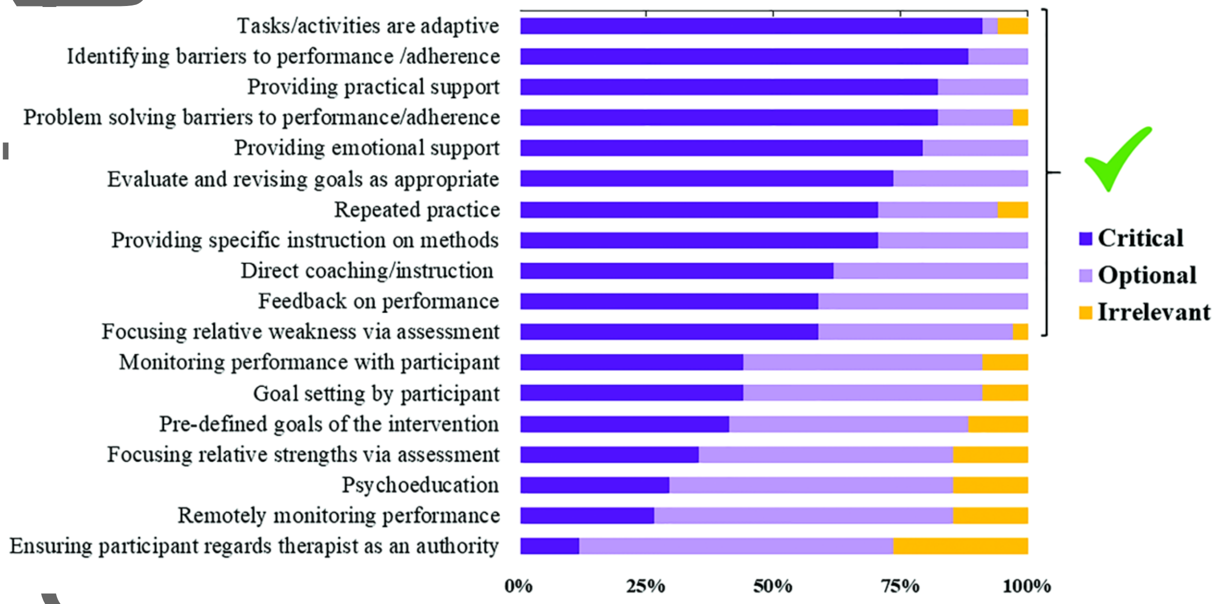


Figure 3. COTs Approaches and Targets

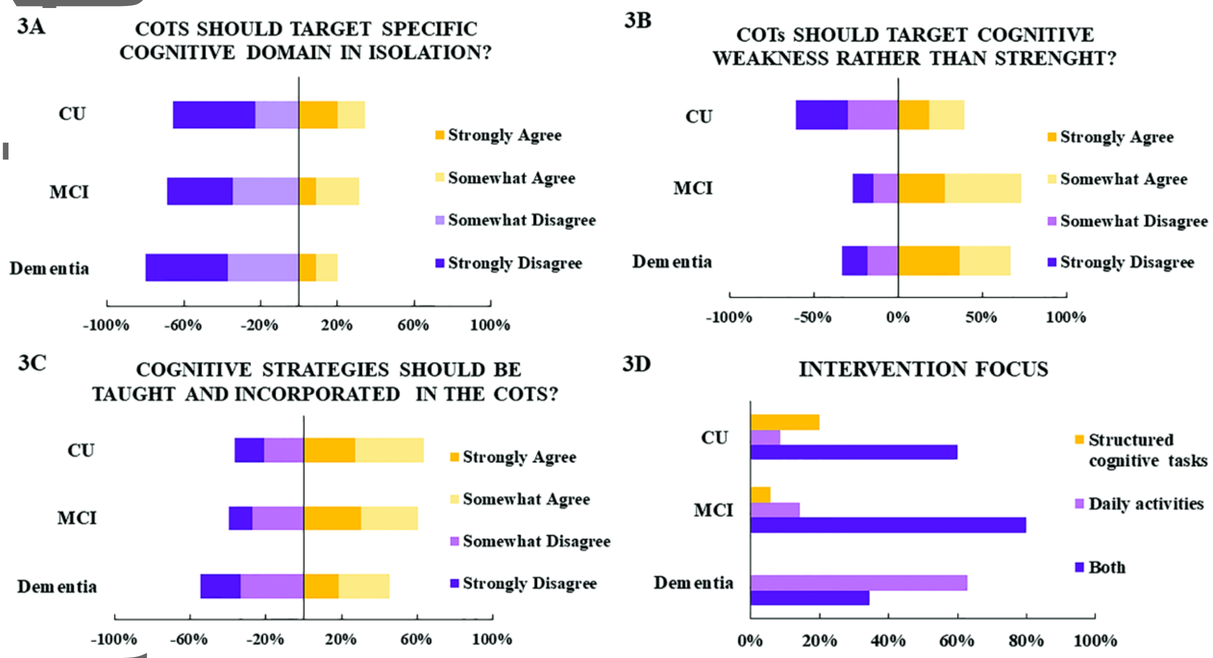


Figure 4. COTs Design

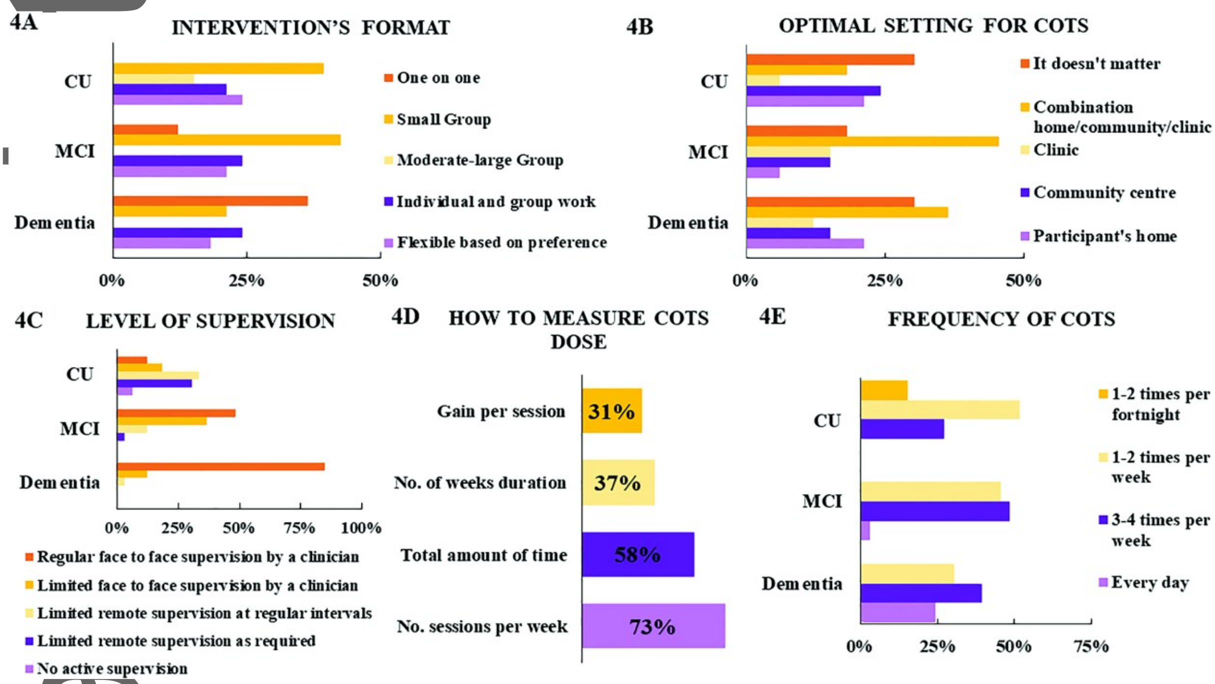


Figure 5. COTs Outcome Measures

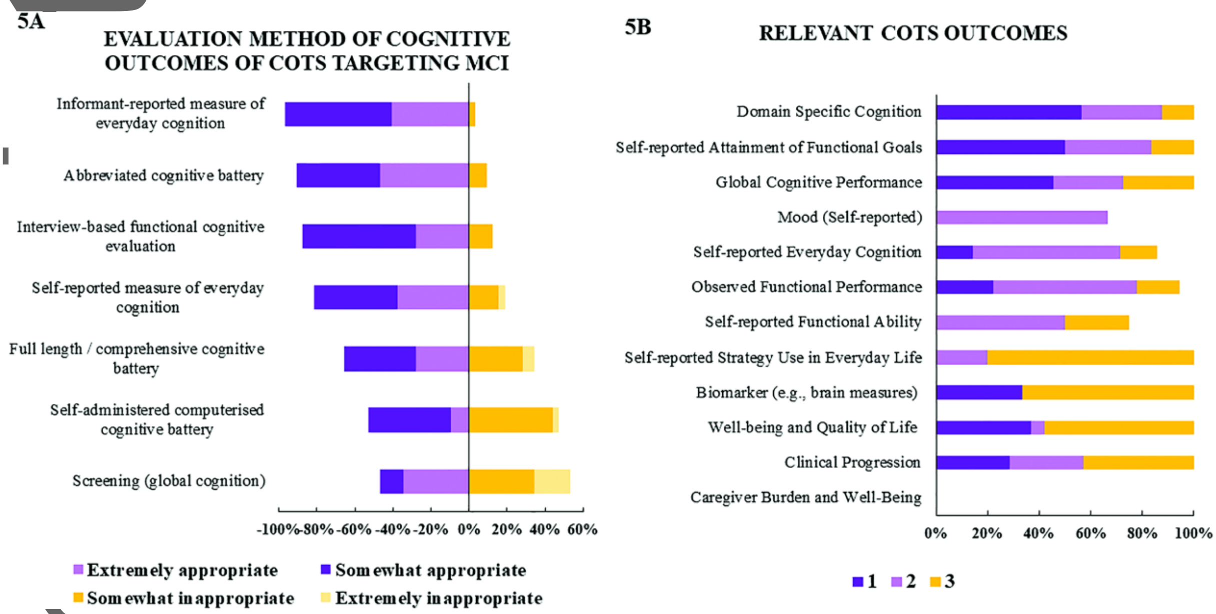


Figure 6. Most Useful COTs Approach for Each Population

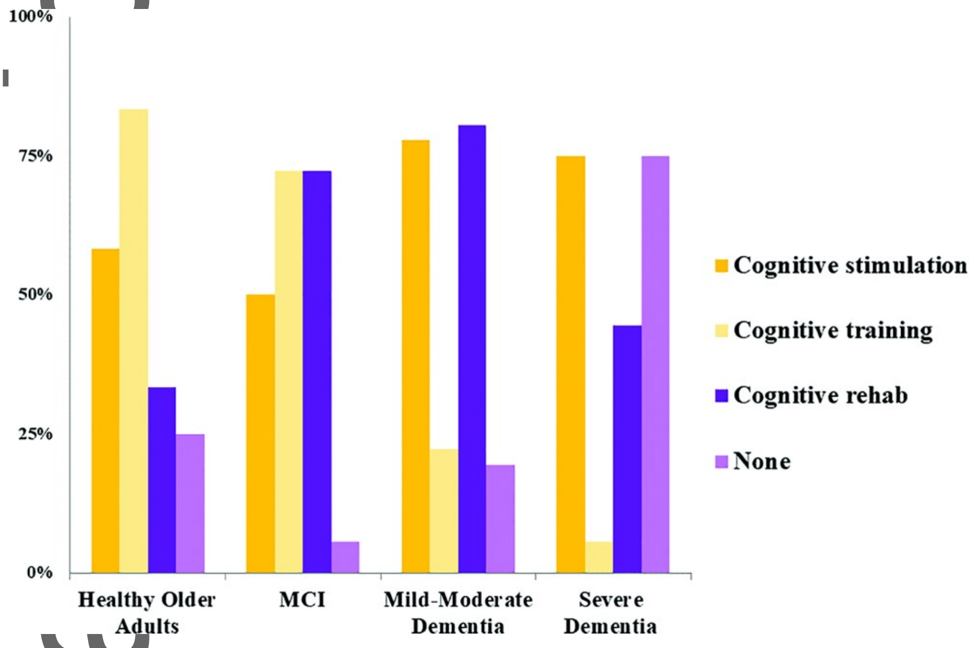


Figure 7. Maintenance of COTs Benefits

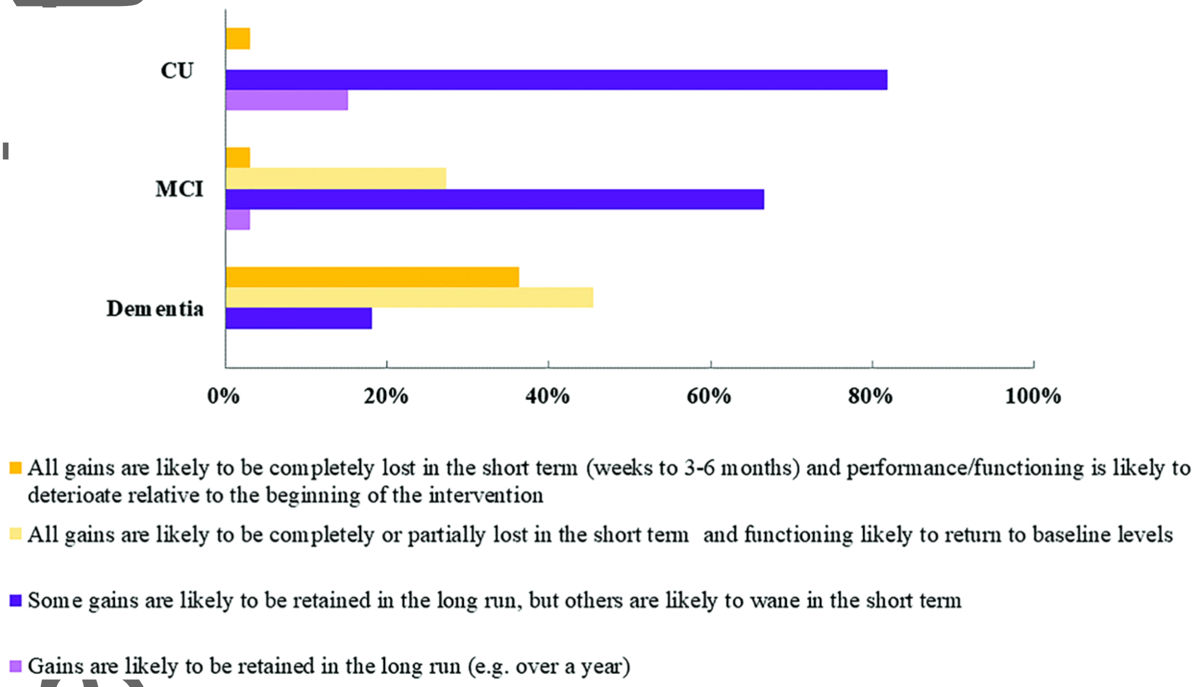
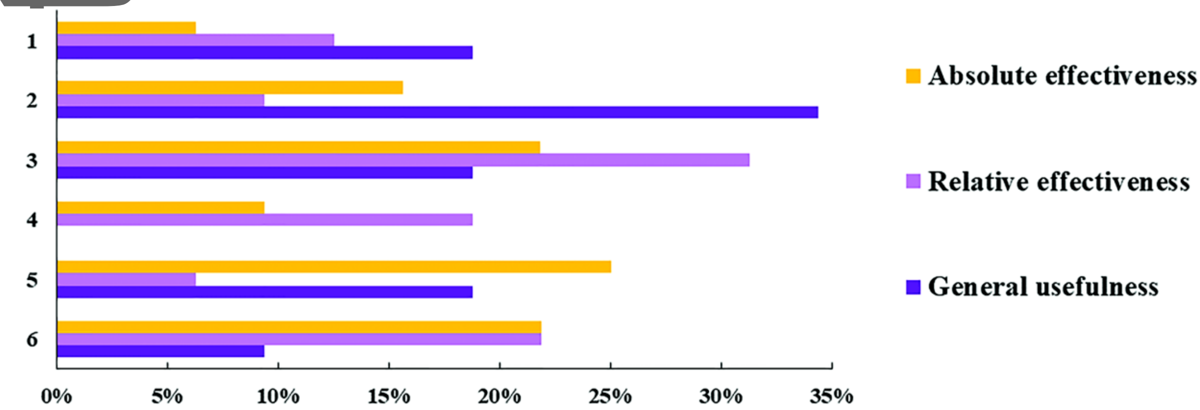


Figure 8. Assessment of Efficacy



1. Superior performance relative to their baseline performance on the outcome in question

2. Greater improvement relative to a "treatment as usual"/waitlist comparison group

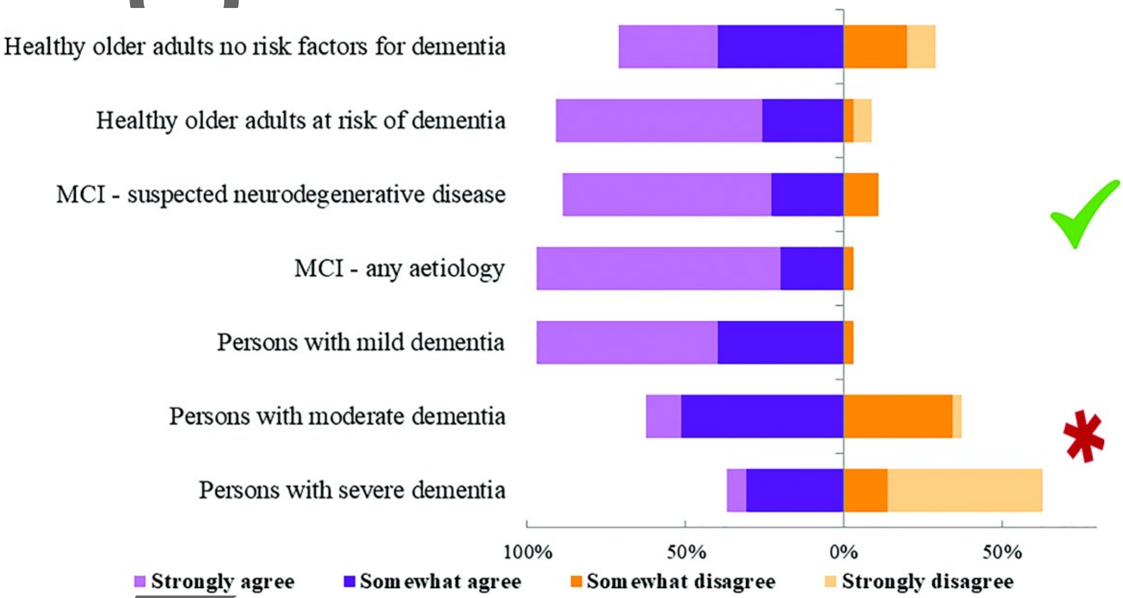
3. Greater improvement relative to a "placebo" or "active" comparison group receiving a treatment similar in all but the "active ingredients"

4. Greater improvement relative to a comparison group receiving another treatment proven to be effective for the same outcome

5. Greater improvement relative to both a "treatment as usual"/waitlist control group and an active or "placebo" condition but not relative to another treatment known to be effective

6. Greater improvement relative to all comparisons, including "treatment as usual"/waitlist control group, an active or "placebo" condition, AND other treatments known to be effective for the particular outcome

Figure 9. COTs Recommendations: In Which Population Should Be Offered?



Survey Topic	General Content[1]
1. Respondent characteristics	Background information, demographics (i.e., age, gender, country), category of professional training and professional experience of the experts.
2. Features and Components	Relevance of cognitive focus (e.g., multiple cognitive domains or in isolation) and approaches, how incorporate strategies and what are the component priorities for effectiveness.
3. Target Population	Specificities of each population targeted in COTs to older adults - CU, MCI or dementia - and likelihood of each to benefit from different COTs.
4. Settings and Mode of Delivery	Importance of type of settings (e.g., clinical, home, community, combined), format (e.g., group, individual, combined) and level of supervision for effectiveness.
5. Dose, Frequency, and Duration	Relevance of number of sessions, intensity per week, trials and minutes engaged in a session, total duration in short- and long-term effects, and role of booster sessions for maintenance.
6. Outcomes and assessments	How measure relevant outcomes, types of cognitive measures/assessments, self-report measures, priorities when considering a relevant outcome for effectiveness.
7. Evaluation of Treatment Efficacy	Ways to demonstrate COT efficacy, control group conditions (e.g., active, 'placebo', waitlist, treatment as usual), between intervention design, level of evidence.
8. Prescription of COTs	Agreement on whether the evidence is strong enough to prescribe particular COT to specific populations.

Table 1. Summary of survey sections

Note: [1]Questions considered the specificity of each population (Cognitively Unimpaired - CU, Mild Cognitive Impairment - MCI and dementia).

Research in Context

1. Survey results & critical review: The authors described the beliefs, attitudes and practices of experts in cognitive oriented treatments (COTs) to older population, and compare with the evidence in the field. The survey identified several areas of agreements among experts on critical features of COTs, study design and outcome measures. Nevertheless, there were some areas with relative disagreement. Critically, opinions were not always supported by scientific evidence.

2. Interpretation: Despite the encouraging results of COTs to older adults, there are inconsistent results in the field that limit the quality of evidence. The findings indicate that methodological improvements in design, implementation and report on COTs is a priority in order to enhance evidence based-practice, dementia prevention and public health recommendations.

3. Future Directions: The manuscript proposes that future COTs research should provide more evidence on dementia prevention. In addition, it is proposed the development of guidelines for COTs research, in order to accelerate the development of high quality evidence of COTs to cognitively unimpaired older adults, those with MCI and dementia.