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Original Study

The Effect of an Online Cognitive Training Package in Healthy Older Adults: An Online Randomized Controlled Trial

Anne Corbett PhD [a], Adrian Owen PhD [b], Adam Hampshire PhD [c], Jessica Grahn PhD [b], Robert Stenton BSc [d], Said Dajani BSc [e], Alistair Burns MD [f], Robert Howard MD [g], Nicola Williams BSc [h], Gareth Williams PhD [a], Clive Ballard MD [a,*]

[a] Wolfson Centre for Age-Related Diseases, King's College London, London, UK
[b] Department of Psychology, University of Western Ontario, Ontario, Canada
[c] The Division of Brain Sciences, Imperial College London, London, UK
[d] Manta Software Ltd, Cambridge, UK
[e] Diabetes UK, Macleod House, London, UK
[f] Institute of Brain, Behaviour and Mental Health, University of Manchester, Manchester, UK
[g] Institute of Psychiatry, King's College London, London, UK
[h] Centre for Statistics in Medicine, University of Oxford, Oxford, UK

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A B S T R A C T

Introduction: Cognitive training (CT) offers a potential approach for dementia prevention and maintenance of cognitive function in older adults. Online delivery provides a cost-effective means of implementing CT compared with in-person interventions, with the potential of providing an effective public health intervention for risk reduction.
Methods: A double-blind 6-month online randomized controlled trial in adults older than 50 randomized to General CT, Reasoning CT, or control. The primary outcome was instrumental activities of daily living (IADL) in adults older than 60. Secondary outcomes were reasoning, verbal short-term memory, spatial working memory, verbal learning (VL), and digit vigilance in adults older than 50. Secondary analyses were performed with a group defined as showing age-associated impairment in reasoning according to baseline scores in this domain.
Results: A total of 2912 adults older than 60 ($6742 > 50$) participated. General and reasoning packages conferred benefit to IADL ($P = .008$, $P = .011$), reasoning ($P < 0.0001$, $P < .0001$), and VL ($P = .007$, $P = .008$) at 6 months. Benefit in reasoning was evident from 6 weeks. Other benefits developed over 6 months. Analysis of participants with age-associated impairment also showed the same pattern of benefit. A clear dose-response effect was seen.
Conclusions: Online CT confers significant benefit to cognition and function in older adults, with benefit favoring the Reasoning package. Scale of benefit is comparable with in-person training, indicating its potential as a public health intervention. Impact on the group with age-associated impairment indicates a particular sensitivity to this at-risk group, which merits further investigation.

Cognitive decline is common among older adults. Although a degree of cognitive loss is a normal part of healthy aging, it also can be a precursor to mild cognitive impairment (MCI) and dementia, a devastating condition characterized by the progressive loss of ability and function leading to incapacity and death. Maintenance of healthy cognition and prevention of cognitive decline and dementia is therefore a key public health issue. The potential impact of a strategy to preserve cognition and delay the clinical onset of symptoms, even by a few months, could be extremely significant from a population perspective and would achieve substantial financial saving at a societal level.[1] There is emerging evidence that interventions aimed

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* Address correspondence to Clive Ballard, MD, Wolfson Centre for Age-Related Diseases, King's College London, London SE1 1UL, UK.
E-mail address: clive.ballard@kcl.ac.uk (C. Ballard).

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at prevention may provide a more realistic opportunity to reduce the burden of dementia in the medium term than disease-modifying therapeutics.[2]

A number of demographic and lifestyle factors affect cognitive change with age,[2] including a growing body of evidence that indicates a role for cognitive reserve in reducing the likelihood of cognitive decline.[3,4] A large recent epidemiological study including more than 13,000 adults older than 65 reported a more favorable cognitive trajectory for people with a higher cognitive reserve score.[5] This raises the question as to the value of specific cognitive training (CT) approaches. Studies in healthy older adults show some promise in improving memory through mnemonic and self-directed memory strategies.[6,7] Although these studies are mostly small, a meta-analysis has indicated a modest significant benefit (effect size 0.16).[8] The consensus indicates that CT may contribute to the delay or prevention of cognitive decline in older adults.[9–11] However, there is only one large randomized controlled trial (RCT) evaluating CT in this group. The Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study investigated the effect of training in several cognitive domains, demonstrating significant improvements in key aspects of cognition such as reasoning (effect size 0.26) and memory (effect size 0.28), which were sustained for up to 10 years.[12,13] The study also showed benefit to activities of daily living. This critical measure of overall function is a key omission in the evidence base, with implications for individuals' independence and the related cost-effectiveness for a population-wide intervention.

A critical aspect of development of a CT package for older adults is the ease of implementation, access, and the cost-effectiveness it provides. Although previous studies provide good proof-of-concept, the most promising interventions have involved intensive in-person sessions that are unlikely to be cost-effective or feasible for large-scale implementation. For example, the ACTIVE study involved 10 focused sessions of up to 75 minutes in which participants were trained in strategies for memory, reasoning, and processing skills. They also received 4 additional booster sessions. If similar benefits could be achieved through an online intervention, millions of people could benefit at a fraction of the cost. A number of computerized, online CT platforms are currently available, although few are underpinned by published evidence. Studies to date are mostly small and focus on cohorts of younger people,[14] although recent studies have shown a generalizable benefit to cognition in older adults, including one study showing similar levels of benefit as in-person training.[15,16] These studies include a computerized package for working memory that improved performance in this domain in 23 older adults and 18 people with amnestic MCI,[17] and an online multitasking game that resulted in sustained improvement in multitasking, attention, and working memory in 46 older adults.[15] Our large study of online CT in 11,430 adults younger than 50 supports the approach, showing high levels of engagement over 6 weeks.[18]

This study evaluates the effectiveness of online CT on cognition in adults older than 50, and on activities of daily living in adults older than 60. The study is based on the hypothesis that online CT focusing on either general cognitive tasks or specific reasoning tasks would confer benefit over 6 months compared with a control.

Methods

Study Design

This was a double-blind 6-month online randomized 3-arm controlled trial. The study compared evidence-based reasoning and problem-solving cognitive training (ReaCT), general cognitive training (GCT), and a control treatment. This study was approved by St Thomas' Hospital Research Ethics Committee (Ref: 09/H0802/85). The protocol is available on the host institution site at http://www.kcl.ac.uk/ioppn/depts/wolfson/about/people/staff/Protocol1.aspx and registered on the International Standard Randomised Controlled Trial Number (ISRCTN) clinical trial database (Ref: ISRCTN72895114).

Participants

All adults older than 50 in the United Kingdom and internationally were invited to take part in this RCT through a partnership with the British Broadcasting Corporation (BBC), Alzheimer's Society (UK), and the Medical Research Council. The trial was publicized through a BBC science education program, "Bang Goes The Theory," on primetime television, and was supported by further publicity via the BBC and Alzheimer's Society, including online and print communication channels. Eligible participants were older than the age of 50, and had access to a computer and the Internet.

Interested individuals were invited to register and consent through a secure connection. This included downloading the information sheet and consenting through an ethically approved online process. Participants then received their unique login details and were randomized to an intervention. Automated e-mails were sent to remind participants to log in and continue their training, as well as completing their online cognitive assessments. A summary of performance and reinforcing text were automatically generated at the end of training sessions.

Treatment Interventions

Two CT interventions were evaluated in comparison with a control intervention. Participants were recommended to undertake the training for 10 minutes daily, although flexibility was allowed. ReaCT focused on 3 reasoning tasks and 3 problem-solving tasks. GCT involved 6 cognitive tasks covering mathematics, attention, memory, and visuospatial ability. GCT tasks were selected for their similarity to components in commercially available products. Details of the specific tasks used in these training packages are provided in Table 1[18] and illustrative images of each task are available online (www.kcl.ac.uk/ioppn/dept/wolfson/about/people/staff/Protocol1.aspx). Task difficulty increased as participants improved so as to maintain the challenge and maximize performance. The control group performed equivalent Internet-based tasks involving a game in which people were asked to put a series of statements in correct numerical order. Participants were invited to search the Internet to find the correct answers. Number of completed sessions per participant was recorded as an integrated feature in the online platform.

Outcome Measures

Outcome measures were completed at baseline (after registering for the trial, but before being shown the training or control tasks) and 6 months, with additional follow-up at 6 weeks and 3 months. Data were collected irrespective of how many sessions the participants had completed. All tests were adapted for use online from publically available validated cognitive assessment tools.[19] The original protocol stipulated an additional 12-month outcome time point, but it was not possible to collect these data because of the loss of server capacity due to a larger than expected number of participants. The 6-month time point was therefore evaluated as the primary outcome.

The primary outcome was self-reported instrumental activities of daily living (IADL) at 6 months in adults older than 60. IADL scoring was completed through the Minimum Data Set–Home Care IADL scale, which has been extensively used in this population.[12,20] IADL data were collected only in participants older than 60 following consultation with patient representatives and an ethics panel, who

Table 1
Training Sessions Included in the ReaCT and GCT Packages Delivered to Respective Treatment Groups

Training Session	Task	Main Outcome Measure
ReaCT		
Reasoning 1	Use weight relationships, implied by the position of 2 seesaws with objects at each end, to select the heaviest object from a choice of 3.	Total number of correct trials across the 2 runs
Reasoning 2	Select the "odd one out" from 4 shapes that varied in terms of color, shape, and solidity (filled/unfilled).	Total number of correct trials across the 2 runs
Reasoning 3	Move crates from a pile, each move being made with reference to the effect that it would have on the overall pattern of crates and how the result would affect future moves.	Total number of correct trials across the 2 runs
Planning 1	Draw a single continuous line around a grid, planning ahead such that current moves did not hinder later moves.	Number of problems completed in 3 minutes
Planning 2	Move objects around between 3 jars until their positions matched a "goal" arrangement of objects in 3 reference jars.	Total number of correct trials across the 2 runs
Planning 3	Slide numbered "tiles" around on a grid to arrange them into the correct numerical order.	Number of problems completed in 3 minutes
GCT		
Maths	Complete simple math sums (eg, 17−9) as quickly as possible.	Total number of correct trials across the 2 runs
Visuospatial	Find the missing piece from a jigsaw puzzle by selecting from 6 alternatives.	Total number of correct trials across the 2 runs
Attention 1	Click on rapidly appearing symbols as quickly as possible, but only if it matched one of the "target" symbols presented at the top of the screen.	Total number of correct trials across the 2 runs
Attention 2	Select numbers in order from the lowest to the highest from a series of slowly moving, rotating, numbers.	Total number of correct trials across the 2 runs
Memory 1	State the number of remaining items of baggage left in an airport x-ray machine after watching a sequence of items moving down a conveyer belt toward the machine. The number of bags going in did not equal the number of bags coming out.	Number of problems completed in 3 minutes
Memory 2	Identify matching pairs of picture cards after being shown the images and the cards being flipped over.	Total number of correct trials across the 2 runs

All sessions consisted of two 90-second "runs."

advised that the content of an IADL scale would not be acceptable to a younger group.

The key secondary measure was reasoning measured as change from baseline in the Baddeley Grammatical Reasoning test in adults older than 50. This test correlates with measures of general intelligence[21] and involves determining the accuracy of a series of grammatical statements about a picture. The outcome measure was the total number of trials answered correctly in 90 seconds, minus the number answered incorrectly.

Other secondary outcomes in all participants were further measures of cognition. Spatial Working Memory (SWM) was measured through the widely used SWM test.[22] Participants searched a series of on-screen boxes to find a hidden symbol. Once found, participants searched for a new symbol, remembering that a symbol would never be hidden in the same box twice. The main outcome was the average number of boxes in the successfully completed trials. Digit vigilance (DV) was measured through a version of the "digit span" task, which has been widely cited in the neuropsychological literature and used in many commercially available brain-training devices.[23] The test used a ratchet-style approach in which each successful trial is followed by a new sequence that is 1 digit longer than the last and each unsuccessful trial is followed by a new sequence that is 1 digit shorter than the last. This allows an accurate estimate of digit span to be made quickly. The main outcome measure was the average number of digits in all successfully completed trials. Verbal short-term memory (VSTM) was measured through the paired associates learning test, widely used in assessment of cognitive deterioration in Alzheimer disease.[24] Participants see a series of objects, one at a time, and select the correct location of each object in "windows" they had previously been shown. The version also used a ratchet-style approach. The main outcome measure was the average number of correct object-place associations ("paired associates") in the trials that were successfully completed. In all tests, participants were allowed 3 errors before the test terminated. VL was measured by change in the recognition score on the revised Hopkin's Verbal Learning Test. There are 6 alternate forms, each containing 12 nouns, 4 words each from 1 of 3 semantic categories to be learned over the course of 3 learning trials, followed by a recognition trial 20 to 25 minutes later composed of 24 words, including the 12 target words and 12 false-positives.

Sample Size

Sample size was calculated based on the standardized effect size (0.26) achieved for reasoning training on reasoning in the ACTIVE study.[12] A total of 442 patients per arm would give a 90% probability that the study would detect a treatment difference at a 2-sided significance level of 0.01 between active treatments and control. To account for any potential dilution of effect due to the online delivery of the intervention and ensure sufficient power in this situation, it was further estimated that the online ReaCT package would have half the effect size of the ACTIVE intervention (0.13). The study therefore required a total of 1763 patients per arm.

Randomization and Masking

Participants were randomly assigned in equal proportions via simple randomization to receive ReaCT, GCT, or control. This was achieved by using a computer-generated randomization sequence to eliminate allocation bias. Participants were blind to which group they were allocated. The online format enabled complete allocation concealment from investigators.

Data Analysis

The primary analysis was intention-to-treat and involved all participants who were randomized. Histograms and normal Q-Q plots were used to visually assess whether outcome data followed a normal distribution. All outcomes were analyzed using a mixed-effects regression model. All non-missing responses were included. Baseline score was entered as a covariate. Missing values were imputed by last observation carried forward for the 6-month outcome for individuals who completed the 3-month outcome assessment. Training outcomes were linearly fitted to training type as predictor variable and the baseline scores as the random effect design matrix: $y_i = A_i x_i + B_n z_{ni} + e_i$, where y_i is the outcome for the i^{th} individual, x_i the

Table 2
Demographic Data for the Cohort at Baseline

Characteristics	ReaCT (n = 2557)	GCT (n = 2432)	Control (n = 1753)
Age, y	58.5 (6.5)	59.1 (6.4)	59.1 (6.6)
Sex, female	1752 (68.5)	1676 (68.9) 2 missing (0.1)	1093 (62.4)
Ethnic origin			
Asian	25 (1)	31 (1.3)	10 (0.6)
Black	7 (0.3)	4 (0.2)	4 (0.2)
Middle Eastern	2 (0.1)	7 (0.3)	4 (0.2)
Mixed race White/Black	8 (0.3)	1 (0.04)	8 (0.5)
Mixed race White/Asian	9 (0.4)	9 (0.4)	11 (0.6)
White	2478 (96.9)	2359 (97)	1707 (97.4)
Other	28 (1.1)	19 (0.8)	9 (0.5)
Missing	0	2 (0.1)	0
Education level			
None	44 (1.7)	55 (2.3)	37 (2.1)
Primary school	14 (0.6)	10 (0.4)	9 (0.5)
Secondary school (GCSE)	400 (15.6)	418 (17.2)	320 (18.3)
Further education (A level)	777 (30.4)	717 (29.5)	556 (31.7)
University graduate/PG	1322 (51.7)	1230 (50.6)	831 (47.4)
Missing	0	2 (0.1)	0
Baddeley Grammatic Reasoning Test	14.4 (5.3) 1 missing (0.04)	14.1 (5.4) 1 missing (0.04)	14.1 (5.3)
SWM Test	5.0 (1.2) 107 missing (4.2)	4.9 (1.3) 80 missing (3.3)	5.0 (1.2) 69 missing (3.9)
Paired Associate Learning Test	3.5 (0.6)	3.5 (0.6)	3.5 (0.6) 1 missing (0.06)
Digit Span Ladder Test	4.8 (1.1) 17 missing (0.7)	4.8 (1.1) 13 missing (0.5)	4.7 (1.1) 9 missing (0.5)

GCSE, general certificate for secondary education; PG, post-graduate.
Values are n (%).

training type, $z_{ni} = 0,1$ assigns the i^{th} individual to the n^{th} baseline outcome group and e_i is the unexplained variance.

Change in scores on all interim time points also were evaluated to provide further information about the time course of effects. Additional post hoc analyses focused on comparison of outcome on cognitive evaluations in all people older than 50 and a separate outcome analysis of all outcome variables focusing on people with age-associated impairment in reasoning (a baseline score <15, 1 SD below the mean value for younger adults[25]). The relationship between outcome and dose was evaluated by calculating the average number of sessions completed by responding and nonresponding participants. All data analysis was performed using Stata Version 12 (Stata Corp, College Station, TX).

Role of Funding Source

The funder supported the collection of data through the online study database. The funder did not have any input into the design of the study, interpretation of results, writing of the manuscript, or decision to publish.

Results

Cohort Characteristics

A total of 6742 adults older than 50 were recruited between August 31, 2009, and November 6, 2009, and randomized. Within this cohort there were 2912 adults older than 60. The mean age of participants in the 3 groups was 65 and more than 60% in each group were women. More than 95% of all participants were Caucasian and more than 40% of people had completed higher education, with a similar pattern in each group. Cohort demographics are summarized in Table 2. The primary trial endpoint was when the last participant completed the last 6-month assessment. Flow of participants through the trial is summarized in Figure 1. Loss of participants at baseline was due to dropout between registration and baseline assessment. Performance on all assessments at baseline was similar across the 3 treatment groups (Table 2). No major deviations that would invalidate the analysis methods used were found.

Impact on Primary Outcome

The ReaCT and GCT packages both conferred significantly greater benefit on the primary outcome measure of IADL than the control treatment at 6 months in those older than 60 (ReaCT: SEM = 0.10, $P = .008$, Cohen D standardized effect size = 0.15; GCT: SEM = 0.11, $P = .011$, Cohen D standardized effect size = 0.16) (Figure 2, Table 3). Data from interim time points also show significant benefit to IADL at 3 months, particularly in the GCT group, although this difference was not significant (Figure 2).

Impact on Secondary Outcomes

In adults older than 50, both the ReaCT and GCT packages conferred significant benefit to reasoning (ReaCT: SEM = 0.16, $P < .0001$, Cohen D standardized effect size = 0.3; GCT: SEM −0.17, $P < .0001$, Cohen D standardized effect size = 0.42) and VL (ReaCT: SEM = 0.11, $P = .008$, Cohen D standardized effect size = 0.18; GCT: SEM = 0.11, $P = .007$, Cohen D standardized effect size = 0.19) at 6 months in comparison with controls. Significant benefit to reasoning was also seen at 3 months, with ReaCT performing marginally better than GCT (Figure 2). Small but significant benefits also were seen in VSTM and SWM with ReaCT (Cohen D standardized effect sizes ≤ 0.1) but not the GCT package compared with the control at 6 months. No benefit to DV was seen at month 6, and a detrimental impact to DV was seen with GCT in comparison to control (standardized effect size −0.11) (Table 3).

Subanalysis: Impact in People With Age-Associated Impairment in Reasoning

A subanalysis was conducted with data from 2873 adults from the main cohort with a baseline reasoning score of less than 15.

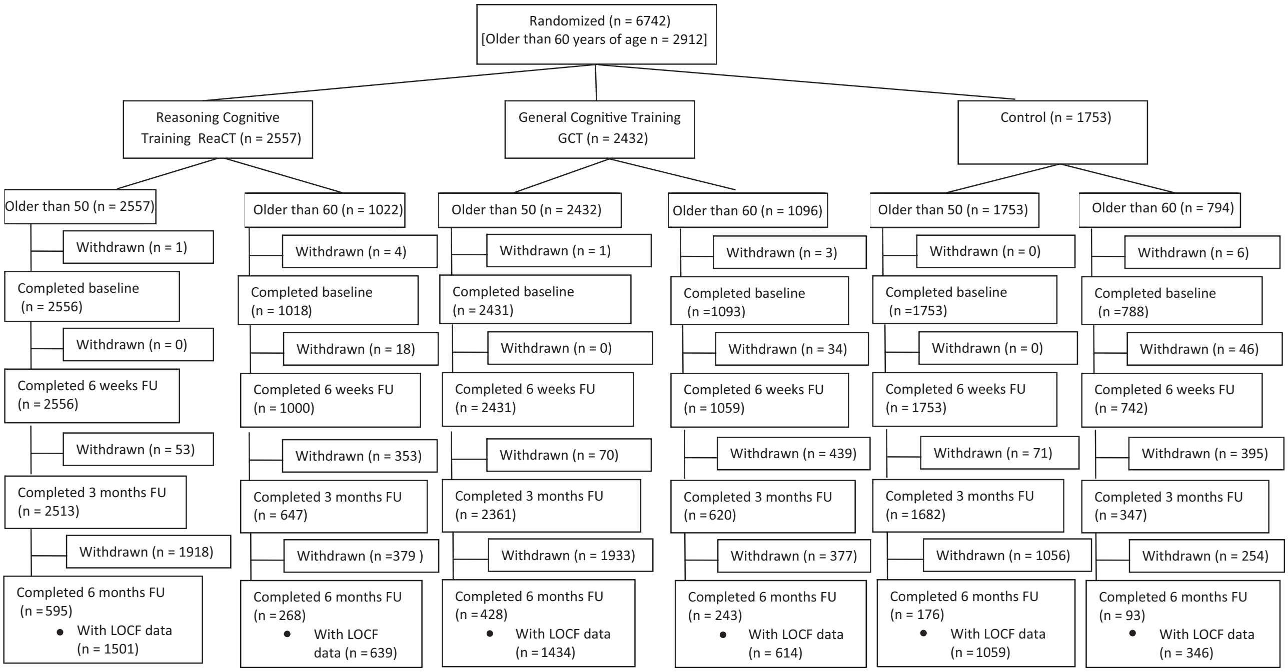

Fig. 1. CONSORT chart showing flow of participants through the study. Note: Reasons for withdrawal are not known due to the online format of intervention and study design. FU, follow-up; LOCF, last observation carried forward.

Similarly to the main cohort, significant benefit was seen in IADL (ReaCT: SEM = 0.14, $P = .027$, Cohen D standardized effect size = 0.17; GCT: SEM = 0.16, $P = .001$, Cohen D standardized effect size = 0.25), reasoning (ReaCT: SEM = 0.25, $P < .0001$, Cohen D standardized effect size −0.46; GCT: SEM = 0.25, $P < .0001$, Cohen D standardized effect size = 0.28), and VL (ReaCT: SEM = 0.14, $P = .039$, Cohen D standardized effect size = 0.19; GCT: SEM = 0.14, $P = .039$, Cohen D standardized effect size = 0.2) at 6 months with both packages, with smaller but significant benefit to VSTM (SEM = 0.04, $P = .14$, Cohen D standardized effect size = 0.1) and SWM (SEM = 0.06, $P = .014$, Cohen standardized effect size = 0.12) with the ReaCT package. The benefit to reasoning and VL was also significant at 6 weeks and 3 months (Figure 2). At the 3-month time point ReaCT also conferred significantly greater benefit than GCT in reasoning (Table 4, Figure 2). A negative impact was seen on DV with both packages in this group (Figure 2).

Secondary Analysis: Impact of Dose on Outcome

A dose-response analysis showed a higher number of completed sessions in IADL responders compared with nonresponders (Responders: Mean = 112.7 [SD 11.2], Nonresponders: Mean = 78.2 [SD 5.9], $P = .01$) for ReaCT, but there was no dose relationship for GCT (Responders: Mean = 72.6 [SD 6.78], Nonresponders: Mean 79.8 [SD 7.6] $P = .47$).

Discussion

This report describes the first very large-scale RCT of an online CT package in older adults. As hypothesized, the data clearly demonstrate a significant benefit to activities of daily living in a group of adults older than 60 receiving both the online GCT and ReaCT interventions compared with control, over a period of 6 months. The standardized effect sizes of 0.16 and 0.15, respectively, are comparable to previously published studies of in-person CT packages in older adults, indicating the efficacy and feasibility of an online approach to CT in this group, and are also comparable to the effect size of cholinesterase inhibitors in mild dementia and cognitive stimulation therapy in studies with a control intervention.[28,29] These findings are novel and extremely valuable since it is known to be difficult to elicit change in IADLs, particularly in a cognitively healthy group. This impact on IADLs therefore indicates the potential for this approach as an effective public health intervention that could improve this key measure of independence and quality of life in older adults.

Additional more substantial benefits were identified in reasoning (effect sizes: ReaCT −0.3, GCT −0.19) and VL (effect sizes: ReaCT −0.18, GCT −0.19). The impact on reasoning in this older cohort is of particular note because this cognitive domain is a key component of executive function. These abilities, which are commonly associated with everyday activities,[12] are frequently the first to be affected in old age, and therefore have particular public health relevance. A published analysis of the baseline performance in the cohort for this study also indicated that age is significantly associated with greater impairment in reasoning, further indicating the importance of this domain.[25] This literature indicates the possible increased potential for improvement in reasoning in older adults, and in this context the findings of this study begin to suggest that the decline in this domain may be remediable.

Analysis of other cognitive outcomes in adults older than 50 also shows a considerable generalizable impact on cognition, with substantial benefits to reasoning and VL in both active CT groups at 6 months, and more modest benefits in SWM. The effect sizes for these cognitive domains exceed those reported by a recent meta-analysis (standardized effect size 0.16), with standardized effect sizes of greater than 0.3 achieved for reasoning and VL. Cognitive benefit was also seen at earlier time points of 6 weeks and 3 months. DV was not affected in the ReaCT group but was negatively affected in the GCT group. Taken together, these findings indicate that the ReaCT package confers a more generalized cognitive benefit than the GCT at 6 months. The lack of impact and negative response in DV was unexpected, but may reflect a tendency for participants to overcomplicate this task because of the parallel increasing complexity of the other reasoning and learning tasks, leading to a drop in performance.

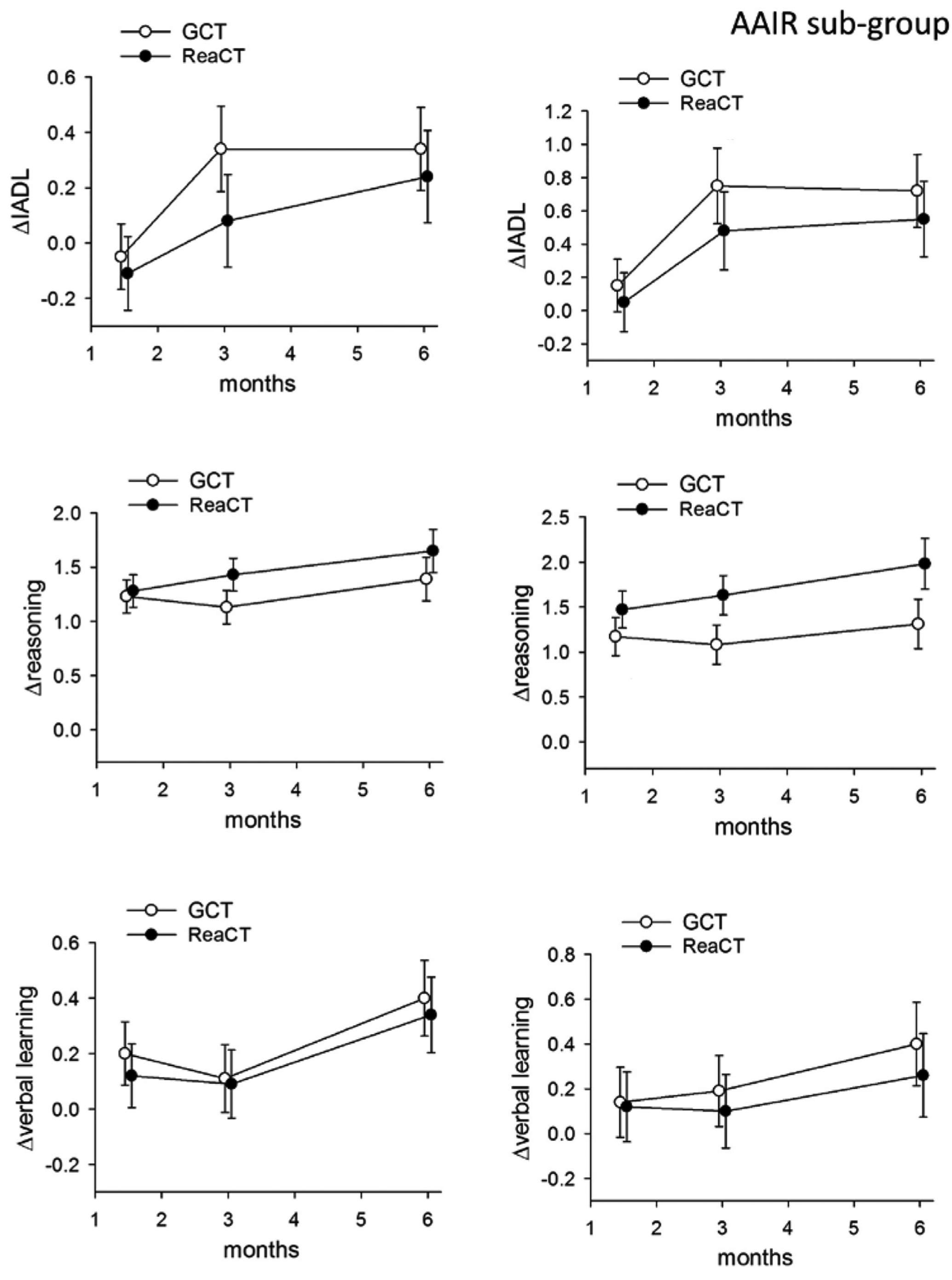

Fig. 2. Change in primary (IADL) and secondary outcomes (Reasoning; VL) in comparison with controls in full cohort and AAIR subgroup at all time points. AAIR, age-associated impairment in reasoning.

A further additional analysis performed in people with age-associated impairment in reasoning showed that the benefit to cognition and IADL was conserved in this group. The thresholds for this analysis applied the concept of age-associated memory impairment, defined as people falling 1 SD below the mean performance of younger adults, specifically to reasoning. It is therefore a potential approach to identify individuals with very early impairments in cognition for interventions aimed at maintaining cognitive health and preventing cognitive decline. Given the current emphasis on targeting very early cognitive deficit in younger populations, these combined findings are particularly exciting.

A final valuable finding from this study is the observation of impact of dose on effectiveness of the CT packages. There was a clear dose-response effect with ReaCT, with responders completing significantly more sessions than nonresponders. On average, responders completed 112 sessions over the 6-month study period, which equates to approximately 5 sessions each week. As part of the ReaCT intervention, we provided a guideline for participants, to complete 3 sessions each week. This finding indicates that this guidance should be increased in future studies to 5 sessions a week to ensure maximum benefit. There was no clear dose relationship for GCT.

Table 3
Comparison of Performance of all Groups in all Outcomes at 6 Months

Training Type	No. Participants in Treatment Group [No. in Control]	Trained		Control		Difference in Mean	SE of Difference in Mean	*P*	Cohen D Effect Size
		Mean	SEM	Mean	SEM				
Primary outcome: IADL (n = 1599)*									
GCT	614 [346]	−0.55	0.08	−0.82	0.07	0.27	0.11	.008	0.16
ReaCT	639 [346]	−0.13	0.08	−0.39	0.06	0.26	0.10	.011	0.15
Secondary outcome: Reasoning (n = 3994)									
GCT	1434 [1059]	−2.6	0.12	−3.89	0.12	1.29	0.17	0	0.30
ReaCT	1501 [1059]	−0.9	0.11	−2.7	0.12	1.80	0.16	<.0001	0.42
Secondary outcome: SWM (n = 5533)									
GCT	2005 [1372]	−0.15	0.02	−0.23	0.03	0.08	0.04	.054	0.07
ReaCT	2156 [1372]	−0.05	0.02	−0.15	0.03	0.1	0.04	.014	0.09
Secondary outcome: DV (n = 5831)									
GCT	2096 [1499]	0.24	0.02	0.37	0.03	−0.13	0.04	.0006	−0.11
ReaCT	2236 [1499]	0.02	0.02	0.06	0.03	−0.04	0.04	.235	−0.04
Secondary outcome: VSTM (n = 3090)									
GCT	1130 [591]	0.01	0.02	0.02	0.03	−0.01	0.04	.845	−0.01
ReaCT	1369 [591]	−0.03	0.02	−0.09	0.03	0.06	0.04	.049	0.10
Secondary outcome: VL (n = 1472)									
GCT	567 [308]	−0.6	0.07	−0.9	0.09	0.30	0.11	.007	0.19
ReaCT	597 [308]	−0.15	0.07	−0.44	0.09	0.29	0.11	.008	0.18

All data presented are analyzed through a Linear Mixed Model.
*IADL data for participants older than 60 only.

This was a large, robust study, and the first to evaluate an online CT approach in older adults. Interestingly, the findings are consistent with previous trials of in-person CT in older adults, but contrast with those of our study in younger adults in which neither CT package showed any impact. This suggests that CT may be specifically beneficial in improving both function and cognition in an older group, perhaps linked to subtle age-related changes in reasoning that the current study suggests can be reversed with CT. Another important factor may be the high level of engagement shown by this older cohort. Comparing the number of completed sessions over the first 6 weeks in this study with our previous study of younger adults, the older adults completed more than double the number of CT sessions than their younger counterparts (mean of 50.7 sessions compared with 24.47 over the first 6 weeks).

There were several limitations to the study. The study included only people with access to computers and was biased toward individuals with higher levels of educational attainment. We do not believe that this is a limitation per se, as it is an opportunity to target a large population of individuals who may best be accessed through an online route, but who may be different from people not regularly using computers. It is, however, important to acknowledge that the results should not therefore be generalized to other populations. There was a significant dropout between months 3 and 6. Loss of engagement has been reported in other recent trials of online interventions (Ballesteros et al[26], Owen et al[27]), and is likely due to the lack of in-person contact within this approach. This study has highlighted the need for optimization of retention strategies beyond the use of automated e-mail prompts, using approaches such as community-based groups to maintain engagement in the intervention. This will be a key focus for future work. The loss of server capacity did not affect the data presented in the current article but did preclude the original planned analysis to examine 12-month outcomes, resulting in a change to the original primary outcome point from 12 months to 6 months.

The implications of the findings of this study for translation to practice are important to consider. The effect sizes in IADL and 2 of

Table 4
Comparison of Performance of Participants With Age-Associated Reasoning Impairment in all Cognitive Outcome Measures at 6 Months

Training Type	No. Participants in Treatment Group [No. in Control]	Trained		Control		Difference in Mean	SE of Difference in Mean	*P*	Cohen D Effect Size
		Mean	SEM	Mean	SEM				
Primary outcome: IADL (n = 910)*									
GCT	358 [207]	−1.01	0.12	−1.52	0.1	0.51	0.16	.001	0.25
ReaCT	345 [207]	−0.16	0.11	−0.47	0.09	0.31	0.14	.027	0.17
Secondary outcome: Reasoning (n = 1958)									
GCT	734 [525]	−2.48	0.18	−3.73	0.18	1.25	0.25	<.0001	0.28
ReaCT	699 [525]	−1.02	0.18	−3.06	0.18	2.04	0.25	<.0001	0.46
Secondary outcome: SWM (n = 2712)									
GCT	1015 [680]	−0.16	0.04	−0.24	0.05	0.08	0.06	.17	0.07
ReaCT	1017 [680]	−0.07	0.03	−0.21	0.05	0.14	0.06	.014	0.12
Secondary outcome: DV (n = 2873)									
GCT	1050 [742]	0.33	0.03	0.5	0.04	−0.17	0.05	.0011	−0.16
ReaCT	1081 [742]	0.06	0.03	0.18	0.04	−0.12	0.05	.02	−0.11
Secondary outcome: VSTM (n = 1612)									
GCT	615 [329]	0.04	0.03	0.07	0.04	−0.03	0.05	.61	−0.04
ReaCT	668 [329]	−0.03	0.02	−0.09	0.04	0.06	0.04	.14	0.10
Secondary outcome: VL (n = 837)									
GCT	335 [182]	−0.6	0.09	−0.9	0.11	0.30	0.14	.039	0.20
ReaCT	320 [182]	−0.15	0.09	−0.44	0.11	0.29	0.14	.039	0.19

All data presented are analyzed through a Linear Mixed Model.
*IADL data for participants older than 60 only.

the cognitive domains (Reasoning and VL) are meaningful, and indicate a potentially clinical benefit. The additional benefit conferred by the ReaCT package also represents a generalized effect that is not seen with GCT, indicating that ReaCT would be most suitable for roll-out. Roll-out of an intervention of this nature would be relatively inexpensive, requiring it to be hosted on a secure Web site, either through a private or public organization, and promoted through health care and public communications. Successful integration as a widely used public health intervention would also rely on close working with professional bodies and targeted communication with health professionals, particularly in primary care, to ensure it became adopted within the health care services. As such, the intervention could be recommended by physicians and promoted as a means of self-directed maintenance of cognition, within the overall advice relating to healthy aging. Further work is needed to explore the best ways to engage individuals over the long-term to maximize effectiveness and impact on public health, but this is likely to require an interactive online presence, perhaps supported through elements of social media and follow-up in primary care. Effective roll-out also would require targeted training for health professionals to ensure referral to the intervention, which could be delivered through existing primary care e-learning approaches. There also is a need to explore the need for close working with policy makers and commissioners of health care services to fully elucidate their potential role in any roll-out endeavor. Policy makers are likely to be central to implementation, with the potential to integrate a brain-training intervention into usual practice in primary care for older adults, and the influence to embed a culture of preventive medicine in public health policy. This may be a beneficial focus of future studies focused on the long-term success and implementation of the intervention.

When translated to a population-wide scale, as would be necessary for an intervention intended to reduce the risk of cognitive decline and dementia, even very small effect sizes translate to extremely significant improvements in overall public health if the reach of the intervention is sufficiently large.[30] When combined with the expected cost-effectiveness of the online format of this intervention, this CT approach, therefore, has great promise as a preventive intervention for older adults internationally that could significantly reduce the burden of the condition.

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