How to train

Participants log into the training website using pre-assigned credientials. Depending on the assigned group, particiants get either CT or AC games. Beside the games playing, user experience were identical between groups. Particiapnts trained 5 session a week, around 42 minutes per session for 10 weeks.

A) Dashboard: User progress this week, start training button

B) Training Levels: Levels to be performed in this session

C) Exercise Overview: Reminder of exercise goals and content

D) Exercise: Perform cognitive training

E) Level Completion: Review progress and performance

F) Session Completion: Review accomplishments from session

Cognitive Training Exercises

All exercises continually adapt task difficulty by changing various aspects of games (e.g., exposure duration, number of distractors, target distractor similarity, etc.) based on participants' performance. This adaptive feature is a critical condition for inducing maximal performance improvement and plasticity of the brain by creating the discrepancy between individual's cognitive ability and environmental cognitive demand. CT exercises apply the adaptivity in three domains, 1) within an exercise, 2) between levels of each exercise, and 3) between distinct exercises. For example, while participants play a 2-3 minutes-long exercise, the exposure duration of stimuli in the exercise gets a little shorter if participants are doing well, and little longer if participants are doing poorly in the level and is continually adjusted so that participants maintain ~75-85% accuracy. Participants get to play the same exercise usually 2-3 times until they reach a certain performance criterion (i.e., a certain amount of improvement from each participant's baseline). When participants repeat the same exercise, the initial difficulty is set by the previous attempt's best performance to promote performance improvement. As levels progress, improvements in speed and/or accuracy and/or higher-order performance operations are challenged at progressively more cognitively demanding levels (e.g., increase the number of distractors, target-distractor similarity, number of items to be remembered, etc.). At the beginning of training, participants start training to improve lower-system-level and modulatory system processes that crucially support higher-level cognition and executive control. As training progresses, participants build on improvements with training exercises targeted to higher-level associative cognitive work such as working memory, episodic memory, and other 'higher-order' neurocognitive abilities.

Adaptivity within level: Exposure duration is adapted by performance.

Watch for a vehicle in the center of the screen and road sign in the periphery.

Respond to the center target and select peripheral target location .

On next trial: Based on the accuracy of the previous trial,

if response is incorrect, increase exposure duration

if response is correct, decrease exposure duration

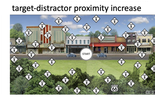
Repeat of the same exercise: The initial exposure duration is set based on the best performance of the previous attempt.

Adaptivity between levels: Task difficulty is increased if participants reached a predefined amount of improvement in the previous level .

Easy level: no distractor

Medium level: number of distractors increases

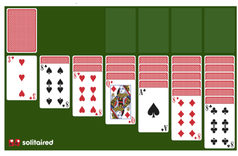
Hard level: number of distractors and target-distractor proximity increase



list of all CT exercises

Active Control Games

We used 12 commercially available computer games designed to: 1) provide a face-valid approach to cognitive training, ensuring participants were blind to group affiliation; 2) match expectation-based influences on performance in cognitive outcomes; 3) match the experimental program in overall program use intensity, staff interaction, reward, and overall engagement; 4) not be continuously adaptive. Three out of 12 games could increase in difficulty within session by discrete levels. The user experience in the AC and CT groups was almost identical except the games played.



list of all AC exercises

Interaction with study staff

Site staff (i.e., training coach) directly interacting with participants during training were not blinded to effectively handle any training-related issues but were instructed to describe each program's features as potentially beneficial. Post-training assessments were administered by staff who were separate from training coaches and blinded to the training condition. The training coach interacted with participants regarding their training only when participants experienced technical difficulties or when participants had an extended period of training absence. If participants had not trained in a week, the training coach sent a standard reminder email. In cases where participants did not respond to the reminder email, the coach called the participant to determine their reason for training absences.

Assessments

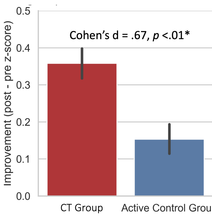
Assessment	Screening (V_0)	Baseline (V_1)	Post-Treatment (V_4)	Follow-Up (V_5)
Informed Consent	X			
Demographics	X			
Medical History	X			
Medications	X	X	X	X
Montreal Cognitive Assessment Task (MoCA)	X			
Columbia Suicide Severity Rating Scale (CSSRS) -Baseline/Screening Version	X			
Inclusion/Exclusion Criteria	X			
Pattern comparison		X	X	X
Letter comparison		X	X	X
Digit Symbol Substitution		X	X	X
Visual working memory		X	X	X
N-back Task		X	X	X
Flanker Task		X	X	X
Face Name Matching Task		X	X	X
Selective Reminding Task (SRT)		X	X	X
Employment/School Status Update		X	X	X
Task Switching (fMRI task)		X	X	X
Timed Instrumental Activities of Daily Living (TIADLs)		X	X	X
Center for Epidemiologic Studies Depression Scale (CESD-20)		X	X	X
Columbia Suicide Severity Rating Scale (CSSRS) –Since Last Visit Version			X	X
Self Efficacy		X	X	X
Perceived Stress		X	X	X
General Life Satisfaction		X	X	X
COVID Questionnaire				X
Survey			X	X

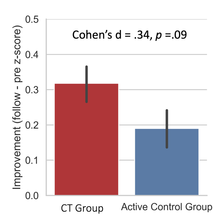
details of assessments

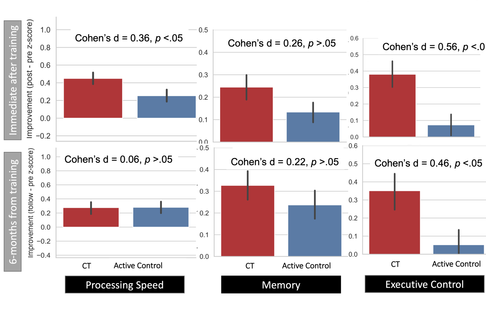
Sample size justification

Based on the results for the overall cognitive composite score change recorded in Phase I, we used DSS research statistical power calculator for a one-tailed test with alpha level at 0.025. That calculation indicated that we will have 93.1% power to test group difference at immediate post training with 132 participants (66 in Cognitive Training, CT and 66 in Active Control, AC). Additionally, given the nature of the study, we anticipate some participant attrition. In intervention research studies conducted earlier by our teams in older adults (including our Phase 1 study), attrition rates are consistently well below 20%. Assuming that there are 52 participants in CT and AC at 6-months post training after 20% attrition, we would still have 86.4% power to test group difference at 6-months follow-up.

CT improved cognitive performance more than AC







CT training results