Study Protocol and Statistical Analysis Plan

Study Title
Examining the Effectiveness of Cognitive Training

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Background

There is a great deal of scientific interest as to whether and how basic cognitive skills can be improved through dedicated behavioral training as this could have substantial real-world impact. A growing body of research has shown that some computerized cognitive training paradigms can benefit at least some aspects of cognition. Recently, it has been proposed that one mechanism through which such gains in cognitive performance could be induced involves participants' expectations of improvement (i.e., placebo effects) as participants cannot remain completely unaware to their training as in other intervention research (e.g., drug trials).

Though placebo effects in other domains have been more extensively examined, the corresponding literature in the cognitive training field has been sparse. No study to date has examined whether it is possible to cause changes in cognitive performance in a long-term cognitive training study by manipulating participant expectations using both an explicit expectation message and an associative-learning (i.e., experience-based) expectation induction. Further, it is unclear whether placebo effects (if any) would persist after unmasking the participants' conditions. However, research from medical domains suggest that at least some placebo effects persist even after patients are made aware of their expectations.

Specific Aims and Hypotheses

This study aimed to examine the extent to which working memory training improves aspects of cognition, the extent to which these effects are augmented by the participants' expectations or placebos, and whether any placebo effects are retained after participants become aware of their assigned expectations among a young adult population (ages 18-30). It was predicted that there would be a main effect of training, such that those who completed the true cognitive training intervention would improve in their cognition overall more than those who completed the control cognitive training, as well as a main effect of expectation, such that those who were given a positive expectation about their training would improve in their cognition overall more than those who received a negative expectation about their training. No interaction between training and expectations was predicted. It was also predicted that both the training and expectation effects would persist after being made aware of their expectations.

Secondary aims included exploring whether individual traits, including demographic characteristics, personality, or motivation, in young adults can predict the strength of placebo effects in cognitive training, and to determine the feasibility of this study with an older adult population (ages 60+). As these were exploratory analyses, no a priori predictions were made.

Study Design

The study design was a 2 (positive expectations vs. negative expectations) x 2 (true cognitive training intervention vs. control cognitive training intervention) between-subjects Randomized Controlled Trial (RCT). Thus, participants were assigned to one of four conditions: Positive expectations with true cognitive training, negative expectations with true cognitive training, positive expectations with control cognitive training, or negative expectations with control

cognitive training. For the older adult feasibility study, only the two true cognitive training conditions with either positive or negative expectations were used.

Recruitment Strategy

Participants for this study were recruited in two phases. The first phase included young adults (ages 18-30), who were recruited via university campus flyer advertisements and university human participant pools at each of the three study sites, University of Wisconsin – Madison, University of California, Irvine, and University of California, Riverside. The second phase included older adults (ages 60+), who were recruited through community flyer advertisements (e.g., senior community centers) and email advertisements to previous lab participants at each site.

Inclusion Criteria:

- Self-reported normal or corrected-to-normal vision
- No known neurological impairments (this includes any neurological impairments that would negatively impact participants' ability to perform perceptual or cognitive tasks or to complete long-term cognitive training; this could include neurological damage due to stroke in various brain areas; seizure conditions that would preclude the ability to view flashing images; motor control issues that preclude the ability to respond via button presses; etc.).
- Access to the internet, a computer, and a hand-held device, such as a cell phone or tablet

Exclusion Criteria:

- Self-reported non-normal or non-corrected-to-normal vision
- Neurological impairments
- No access to the internet, a computer, or a hand-held device

Procedure

Participants were first screened via email (young adults) or phone (older adults) to ensure they met all eligibility criteria. Young adults self-reported that they met eligibility criteria, while older adults were screened using the Montreal Cognitive Assessment Short – Abbreviated Telephone Version (MoCA), Geriatric Depression Scale – Short Form (GDS), and Geriatric Anxiety Scale – 10 Item Version (GAS).

During the first set of sessions, participants provided consent via an online form and then completed a pre-test cognitive battery (see Dependent Measures) online with a researcher present via Zoom. They also filled out a set of surveys about demographic information, personality traits, and other internal dispositions that may predict the extent to which they are susceptible to placebo effects.

After the pre-test, participants were assigned to their expectation group (positive/negative) and their training group (active/control), which was randomized prior to the start of the study. They were first given their group appropriate explicit expectation presented in a series of paragraphs and images online. Those in the positive expectation group were told that the training that would

complete has previous research supporting its use as a method to enhance cognitive abilities. Those in the negative expectation group were told that the training they would complete has previous research suggesting that it is unlikely to change cognitive abilities or may even decrease participants' scores on the tests of cognitive function. Note that depending on the participants' particular training group assignment, this may or may not have been deceptive. If they were assigned to the true cognitive training intervention, there is research showing that the to-be-utilized true training increases cognitive function. As such, those that received positive expectations received accurate information and those that receive negative expectations received inaccurate information. However, there is no research showing that the control training intervention increases cognitive function. As such, those that received negative expectations received accurate information and those that received positive expectations received inaccurate information.

The participants were then given instructions on how to complete their training task. Participants were asked to complete ten 20-minute sessions of training once per day without the presence of a researcher. The true cognitive training intervention was standard working memory (*n*-back) training task. In this task, participants were shown a series of colored circles one after another. As each circle appeared, their task was to indicate whether the color matched the one presented *n*-items back in the stream by tapping on the circle. For example, if they were performing a 3-back level, if they had seen the in the colors red, blue, green, and red, and then they saw the color blue, they would tap the screen. The control training intervention was a trivia/quiz task, which included general trivia questions.

After they completed 10 training sessions, they completed a "mid-test" session to complete a cognitive battery online with a researcher via Zoom. They were told that they would complete this cognitive battery as a “check-up” to see how their cognition had been changing during the study, and they were not told that it would be any different than the pre-test. However, in reality, for participants in the positive expectations groups, these tasks were altered to be easier than they were at pre-test to give the impression of cognitive improvement. For participants in the negative expectations groups, the tasks were made more difficult to give the impression of no change/degradation in cognition.

Participants were then asked to complete another set of 10 training sessions without the presence of a researcher before completing a post-test cognitive battery. All participants were then extensively debriefed; all deceptions were made clear, and participants were given an opportunity to ask any questions about the purpose of the study. About a week later, participants completed the cognitive battery one last time to examine whether any changes in cognitive function that were seen in the post-test persisted after the participants were informed about their expectations.

Study Timeline

Session(s)	Description	Approx. Day(s) of Study*
1	Cognitive battery pre-test Part 1	1
2	Cognitive battery pre-test Part 2 Individual difference questionnaires	2
3	Explicit expectation induction Training intervention instructions	3
4 -13	Cognitive training sessions Part 1 (20 min x 10 sessions; once per day)	4-13
14	Associative-learning cognitive battery "mid-test"	14
15 – 24	Cognitive training sessions Part 2 (20 min x 10 sessions; once per day)	15-24
25	Cognitive battery post-test Part 1	25
26	Cognitive battery post-test Part 2	26
27	Debriefing	27
28	Cognitive battery delayed-test Part 1	34
29	Cognitive battery delayed-test Part 2	35

*The length between study sessions varied across participants. 35 days was the minimum length to complete the study.

Dependent Measures

The main dependent measure consisted of a 12-task cognitive battery, 2 of which are control measures. Each of the tasks are described below.

1. The *n*-back task is a working memory measure in which participants view a series of letters and are asked to indicate whether the current letter is the same as the letter *n* items back. The *n*-back levels will vary between 1- and 3-back.
2. The O-Span task is a working memory measure in which participants alternate between completing simple math problems (e.g., 3+(2x2)) and viewing single letters. At the end of a given sequence, the participants are asked to recall all the letters that they had seen in the correct order. The number of letters to be recalled will range between 3 and 7.
3. The Task-Switching Task measures cognitive flexibility. On each trial, participants view a letter and a digit. The location of the pair instructs the participants to either categorize the letter as a consonant or vowel or else categorize the digit as even or odd.
4. The countermanding task is a cognitive flexibility task in which participants are presented with two types of stimuli on either the right or the left side of the screen and are required to tap on one of two buttons on either the same side as the stimulus or the opposite side of the stimulus.
5. The Useful Field of View (UFOV) is a measure of visual selective attention. Participants are briefly presented with a display consisting of a number of items on each of the four radial spokes and the four obliques; evenly spaced. One of the items is a target, while the remaining items are distractors. The participants' task is to indicate upon which of the 8 spokes the target appeared.

6. The Attentional Network Test (ANT) measures visual selective attention. On each trial, participants view a center arrow that faces either left or right. The arrow can be flanked on either side by either response compatible arrows (i.e., arrows facing in the same direction as the center arrow) or response incompatible arrows (i.e., facing the other direction). The participants' task is to indicate the direction that the center arrow is pointing.
7. The Mental Rotation Task measures spatial cognition. Participants are shown two images side by side. The images are either identical, but with one rotated relative to the other, or are mirror-reversed and rotated copies of one another. The participants' task is to indicate whether the two items are identical or are mirror-reversed copies.
8. The paper-folding task is a spatial cognition task in which the participant is shown a depiction of a piece of paper being folded various ways before a hole is punched in the paper. The participants' task is to indicate what the paper will look like when it is unfolded.
9. Raven's Advanced Progressive Matrices (RAPM) is a fluid intelligence measure in which the participant is presented with a grid of elements with one of the elements missing and is asked to identify the missing element that completes the grid pattern.
10. The UC Matrix Reasoning Task is a fluid intelligence measure, similar to RAPM, in which the participant is presented with a grid of elements with one of the elements missing and is asked to identify the missing element that completes the grid pattern.
11. The Mill-Hill Vocabulary scale is a control measure that assesses vocabulary ability.
12. The Shipley Institute of Living scale is also a control measure that assesses vocabulary ability.

Secondary measures used to determine whether individual characteristics predict placebo effects in cognitive training included demographic variables (e.g., age, gender, race/ethnicity), Big Five Inventory (BFI-10), Work and Family Orientation Scale (WOFO), Grit, Behavioral Avoidance/Inhibition scales (BIS/BAS), Theories of intelligence, Schutte Self-Report Emotional Intelligence Test, and Meta-Cognitive Skills Scale.

Statistical Analysis Plan

To examine the main hypotheses, a 2 (true cognitive training vs. control training) x 2 (positive expectation vs. negative expectation) MANCOVA will be conducted on the set of 10 dependent post-test variables, with pre-test scores as a covariate. Scores will be standardized prior to analysis. If significant, post hoc analyses will be conducted as necessary (i.e., it is unlikely that every DV will be similarly impacted by placebo effects - as such, follow-up analyses separated by DV will be performed after the main analysis). A similar analysis will be conducted on the delayed test scores (controlling for pre-test scores).

The following secondary variables will be analyzed to test for moderation of placebo effects on each DV: Big Five Inventory (BFI-10) subscale scores, Motivation (BIS/BAS) subscale scores, Grit scale score, Metacognitive scale score, Fixed/growth mindset scale score, Schutte Self-Report Emotional Intelligence Test subscale scores, Work and Family Orientation subscale scores, Demographic variables, such as age and gender.