

SUPPLEMENTAL MATERIAL

Data S1.

Supplemental Methods

The exercise training portion of the study was overseen by Dr. Tiozzo, who has a Ph.D. in exercise physiology. All team members involved in the exercise portion of the study went through training sessions with Dr. Tiozzo on proper protocol and training procedures, and had either an exercise physiology background, or were on a pre-med or exercise physiology degree track. Cognitive training was carried out by the coordinator or study team members who had been trained on the protocol and undergone practice sessions with the coordinator prior to administering the cognitive training. Trainers were overseen during the first few sessions to ensure a thorough understanding of proper training procedures. All cognitive assessments were performed by the coordinator who was trained and then approved by Dr. Loewenstein on the administration of the neuropsychological test battery.

Table S1. Cognitive Training.

Computerized training was done through Posit Science (San Francisco, California). Programs were selected based on their ease of use for these age groups, and the adaptability of the programs to each participant's current level of function. Specifically, these computerized programs adjust to the level of difficulty according to the individual's performance by increasing the number of stimuli, decreasing stimulus presentation time or response time, or increasing working memory demands. These programs have a strong track record of use in clinical trials.⁵⁻⁷ (for additional details please access: <https://www.brainhq.com>). Specific training components are as follows:

Visual Attention

Target Tracker (Posit Science). The participant must keep track of one or multiple arrays of moving targets with an increasing number of targets added to increase complexity. Speed of the targets and contrast change as different levels of proficiency are met.

Double Decision (Posit Science): This is a modification of the road tour useful field of view (UFOV) Training Program, initially used in the ACTIVE Trial to improve visual processing speed and ability to use visual information in a divided-attention format.⁵ Participants have to choose which of two objects (cars) they saw after one appears briefly in the middle of the screen. But at the same time, they have to notice where a Route 66 road sign appears in the periphery of the screen. Speed of the targets change as different levels of proficiency are met.

Processing Speed

Eye for Detail (Posit Sciences). This task requires the participant to make saccades more quickly, and to notice subtle details of targets with each one. Three to five images briefly appear one at a time in different positions on the screen. As the subject becomes more proficient they flash by quicker. Some of the pictures are similar but not the same while others match perfectly.

Fine Tuning (Posit Science)

This task produces two similarly sounding targets at different speeds requiring the participant to discriminate between the targets and to enhance auditory processing speed.⁶

Working Memory

Scene Crasher (Posit Science). Participants are required to train their visual working memory by quickly taking in and remembering the details of a scene. In the exercise, the participant will see several items (such as sheep or keys) flash on screen. After they disappear, they reappear—but with one additional item. The task is to remember the scene from the first flash well enough to spot what changed when it reappears.

Executive Function

Card Shark (Posit Science). Participants are presented with playing cards that are added one at a time to a sequence. Once presented, the card is turned over. Their task is to decide if the current card matches the card presented a specific number of steps back in the sequence.

Juggle Factor (Posit Science). Participants are presented with a sequence of numbers that are placed within moving circles. Their task is to reconstruct the sequence in the right order and in the right locations. The number of items in the sequence grows as they improve at the task. As they progress through training, the moving object trajectories become more complex and the speed increases.

Table S2. Neuropsychological assessments at baseline and 3 months follow up.

Test	Intervention Arm (tot n =131)	Baseline Score	3-month follow-up Score
HVLT total recall, mean (SD)	Intervention (n=86)	19 (6)	22 (6)
	Control (n=45)	19 (6)	22 (8)
HVLT delay recall, mean (SD)	Intervention (n=86)	6 (3)	7 (3)
	Control (n=45)	6 (3)	7 (3)
HVLT recognition/discrimination index, mean (SD)	Intervention (n=86)	9 (3)	9 (2)
	Control (n=45)	9 (3)	10 (2)
BVMTR total recall, mean (SD)	Intervention (n=86)	16 (9)	20 (8)
	Control (n=45)	18 (10)	21 (10)
BVMTR delay recall, mean (SD)	Intervention (n=86)	6 (4)	7 (3)

	Control (n=45)	6 (4)	8 (4)
BVMTR copy, mean (SD)	Intervention (n=86)	11 (2)	12 (1)
	Control (n=45)	11 (2)	11 (3)
WAIS digit symbol, mean (SD)	Intervention (n=86)	34 (17)	37 (18)
	Control (n=45)	32 (18)	32 (23)
Digit span backwards correct, mean (SD)	Intervention (n=86)	4 (2)	5 (2)
	Control (n=45)	4 (2)	5 (3)
D-KEFS inhibition uncorrected, mean (SD)	Intervention (n=86)	3 (6)	3 (5)
	Control (n=45)	3 (5)	2 (2)
D-KEFS color naming uncorrected, mean (SD)	Intervention (n=86)	1 (3)	0.3 (0.7)
	Control (n=45)	1 (3)	0.2 (0.5)

D-KEFS color naming time to complete, mean (SD)	Intervention (n=86)	49 (18)	44 (18)
	Control (n=45)	47 (16)	44 (15)
D-KEFS inhibition/switching time, mean (SD)	Intervention (n=86)	109 (44)	98 (39)
	Control (n=45)	101 (35)	103 (40)
Cogstate corrected one back, mean (SD)	Intervention (n=86)	25 (9)	26 (9)
	Control (n=45)	25 (9)	25 (9)
Cogstate error one back, mean (SD)	Intervention (n=86)	14 (11)	14 (13)
	Control (n=45)	15 (13)	14 (14)
Cogstate speed one back, mean (SD)	Intervention (n=86)	3 (0.4)	3 (0.1)
	Control (n=45)	3 (0.1)	3 (0.6)
	Intervention (n=86)	23 (10)	26 (9)

Cogstate corrected two back, mean (SD)	Control (n=45)	25 (9)	24 (9)
Cogstate error two back, mean (SD)	Intervention (n=86)	17 (9)	18 (14)
	Control (n=45)	18 (11)	17 (12)
Cogstate speed two back, mean (SD)	Intervention (n=86)	3 (0.4)	3 (0.2)
	Control (n=45)	3 (0.1)	3 (0.1)
Cogstate set shifting corrected, mean (SD)	Intervention (n=86)	112 (22)	115 (19)
	Control (n=45)	111 (25)	107 (28)
Cogstate set shifting error, mean (SD)	Intervention (n=86)	56 (20)	58 (20)
	Control (n=45)	51 (17)	51 (15)
Cogstate set shifting speed, mean (SD)	Intervention (n=86)	3 (0.3)	3 (0.3)
	Control (n=45)	3 (0.2)	3 (0.3)

HVLT - Hopkins Verbal Learning test; BVMTR- Brief Visuospatial
Memory Test Revised; DKEFS- Delis-Kaplan Executive Function system, WAIS- Wechsler
Adult Intelligence