

study's main outcome. Older adults' living arrangements are an example of the interdependency of people and their environment. Individuals' family coping skills are responsible for an appropriate response to a stressful event such as hospitalization. Nevertheless, the requirements and resources of the household could be modified upon one of its member's hospital admission. The results of the present study suggest that the comprehensive approach of acute geriatric wards could neutralize the effect of social vulnerability on health-related outcomes since professional care secures differential demands. Further study could establish the effect of living arrangements on the success of transitions from hospital to home and on the risk of readmission, to better understand the role of living arrangements as a social determinant of health.

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EFFECT OF COGNITIVE TRAINING TARGETING ASSOCIATIVE MEMORY IN THE ELDERLY: A SMALL RANDOMIZED TRIAL AND A LONGITUDINAL EVALUATION

To the editor: Memory decline is considered an aspect of normal aging.¹ However, cognitive training can decelerate or reverse age-related memory loss. Although the effects of cognitive training have been evaluated in several controlled trials,²⁻⁵ there is a lack of longitudinal analyses monitoring cognitive gains over the duration of treatment. In the current study we present a small randomized controlled trial incorporating both a pre-post assessment and a longitudinal analysis of cognitive change. We hypothesized that frequent cognitive training induces gradual cognitive gains over the duration of the training program.

We created two computerized complex matching tasks known to induce equivalence relations and other forms of complex discriminative learning.⁶

WORD-IMAGE MATCHING

In this task we presented random words at 1-second intervals. Subsequently, we presented pictures matching these words along with distractors. The number of target stimuli per trial (3-7) and the target-distractor ratio (1:3-1:7) increased gradually over 10 successive trials. Participants were asked to select the pictures matching the words in both direct and reverse presentation order (outcome: number of correct responses per session).

ANIMAL-SHAPE MATCHING

During this task we presented a two-by-two matrix with five animal-shape pictures (e.g., dog within a triangle) in every cell. The location of the animal-shape compound and the orientation of the shape changed from cell to cell and from trial to trial. During five training trials participants were asked to select the cell containing an animal-shape compound that was not present in any of the other cells. After the training trials, participants were asked to match shapes with animals (outcome: number of seconds to complete the task).

Our two cognitive training tasks were not designed after any commercially available neuropsychological test (see bme.ee.umanitoba.ca/BrainExercises). Stimulus location, order, and stimulus relations varied randomly across task administrations in order to prevent practice effects.

PARTICIPANTS & INTERVENTION

Twenty-four cognitively intact older adults living independently were randomly assigned to a cognitive training group (n = 13; mean age: 78.3 ± 6.5; 11 women) or a control group (n = 11; mean age = 75.18 ± 4.6; eight women). Groups had comparable age, gender distribution, and cognitive function (Montreal Cognitive Assessment) (Mann-Whitney, *P* > .05). Training consisted of 30-minute sessions of Word-Image and Animal-Shape Matching tasks, three times per week, for 8 consecutive weeks.

We administered the Wechsler Memory Scale 3rd ed. (WMS) immediately before and after training. We also

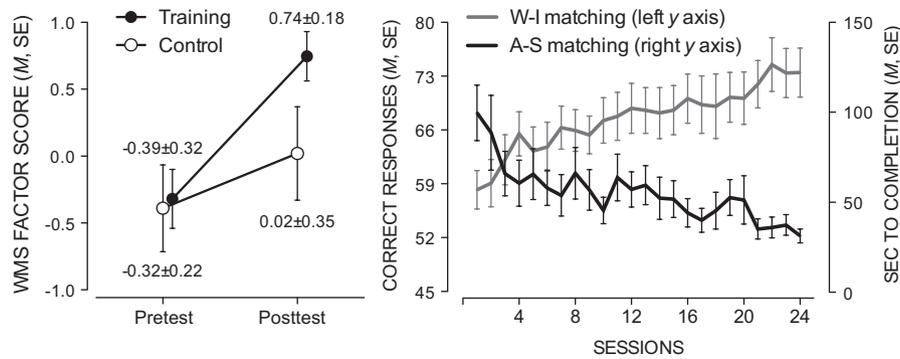


Figure 1. Pretest and posttest evaluation (left graph), and longitudinal evaluation (right graph) of a short-term cognitive training program for older adults. A-S matching = Animal-Shape Matching; W-I matching = World-Image Matching; WMS = Wechsler Memory Scale, 3rd ed. All outcomes reported in mean (M) and standard errors (SE).

administered the WMS twice to the control group, 8 weeks apart. The assessments were administered concurrently across groups. Those administering the assessments were blind to group assignment.

PRE-POST ANALYSIS

We used a two-factor analysis of variance (ANOVA) with time of assessment (pre-test, post-test) as within-subject factor and group (control, training) as between-group factor. The dependent variable was the factorized score of all WMS outcomes resulting from the unidimensional solution of an unweighted least squares factor analysis.⁷ The Bartlett's statistic ($P < .05$) and the Kaiser-Meyer-Olkin test ($> .5$) supported the adequacy of the correlation matrix. Goodness of fit parameters (mean fitted residuals: $< 1/(n^{1/2})$, root mean square residuals ($< .06$), and parallel analysis supported the unidimensional solution.⁸

LONGITUDINAL ANALYSIS

We used unconditional multilevel models for the longitudinal analysis of the individuals' performance in the training group. Training session number served as time variable, and correct responses and seconds-to-task completion served as outcomes for Word-Image and Animal-Shape Matching, respectively. We computed level-1 parameters including intercept (initial status), slope (rate of change per session), and within-person variance.

Factor analysis was conducted with Factor 9.29.^{9,10} All other analyses were conducted with STATA v. 11 (College Station, TX) and its GLAMM program for multi-level analysis.

Participants in the training group increased their memory performance relative to the pre-test assessment established by the WMS factor (Figure 1). Consistent with our hypothesis, the ANOVA revealed a significant interaction between group and time of assessment, $F_{1,25} = 7.55$, $P = .0117$, while the main effect of group assignment was not significant ($P > .1$). The longitudinal analysis showed a significant effect of training session number over performance change during training (Word-Image: $\gamma_{WI} = 0.45$, 95%CI 0.37, 0.53, $P < .001$; Animal-Shape: $\gamma_{WI} = -1.69$, 95%CI $-2.51, -0.87$, $P < .001$).

These findings suggest that short-term cognitive training in the form of complex discrimination tasks can induce significant and gradual memory gains in older adults. Further studies are necessary to determine the impact of cognitive training using outcomes of greater ecological validity (e.g., use of memory during daily living activities). Also, longitudinal analyses of a wider time scale could help to determine the extent to which cognitive training can decelerate or reverse age-related memory decline and other forms of cognitive impairment such as dementia.

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Author Contributions: Ms. Mari Tere Garcia-Campuzano developed the initial project proposal, led the data collection process, and wrote the first version of the manuscript. Dr. Javier Virues-Ortega designed and conducted the analyses and wrote the final version of the manuscript. Dr. Steven Smith consulted on the neuropsychological assessments and provided feedback on the various versions of the manuscript. Dr. Zahra Moussavi provided technical and institutional assistance for the development of the cognitive training tasks and the implementation of the study, and provided direct advice to the first author throughout all the stages of the study.

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CASE REPORTS

MYOPATHY AFTER SWITCHING FROM BRAND TO GENERIC ATORVASTATIN

To the Editor: Statin-induced myopathy poses a significant barrier to optimizing cardiovascular risk reduction for individuals with dyslipidemia, particularly elderly adults.^{1,2} Herein is reported an individual with unusual presentation of statin-induced myopathy.

A 70-year-old Caucasian man with a past medical history of hyperlipidemia presented to the endocrinology clinic in November 2012 for routine follow-up. He complained of

progressively worsening myalgia over the previous 3 months involving shoulders and quadriceps bilaterally. His other past medical history included type 2 diabetes mellitus, hypertension, diabetic kidney disease, carotid artery stenosis treated using right endarterectomy, hypothyroidism, and vitamin D deficiency. He was taking insulin glargine 12 U/d, sitagliptin 100 mg/d, atorvastatin 10 mg/d, amlodipine 2.5 mg/d, metoprolol extended release 100 mg/d, candesartan 8 mg/d, ramipril 5 mg/d, aspirin 81 mg/d, levothyroxine 112 µg/d, and vitamin D₃ 5,000 IU/d.

He had been treated with brand-name Lipitor (Pfizer Inc, New York, NY) at a dose of 10 mg/d for the past 8 years. At the time of evaluation in the clinic, he denied recent use of over-the-counter medications or changes in prescription medications including antibiotic use, dehydration, or any changes in physical activity level or exercise pattern. He had no history of alcohol or tobacco abuse or recreational drug use. His body mass index was 25.5 kg/m², and physical examination was unremarkable.

Laboratory testing during the clinic visit revealed a low-density lipoprotein cholesterol (LDL-C) level of 73 mg/dL, a creatine kinase (CK) level of 1,397 U/L (normal range 24–200 U/L), and an aspartate aminotransferase (AST) level of 74 U/L (normal range 0–40 U/L) (Table 1). Glycosylated hemoglobin was 6.0%, and plasma creatinine concentration was unchanged since his last visit (1.28 mg/dL). His vitamin D and thyroid-stimulating hormone levels were within the normal range at 42 ng/mL and 1.62 µIU/mL, respectively. Erythrocyte sedimentation rate and C-reactive protein levels were normal at 2 mm/hour and 0.3 mg/L, respectively. Creatine kinase (CK) and AST levels had been normal in the previous months (Table 1). With the new diagnosis of myopathy, the statin was discontinued. Over the course of the following 2 months, his CK and AST levels normalized, although as expected, his LDL-C and total cholesterol increased (Table 1). Investigations revealed that he had been switched from brand name to generic atorvastatin manufactured by Ranbaxy Pharmaceuticals Inc. (Ranbaxy, Princeton, NJ) in April 2012. Therefore, with the resolution of his symptoms and normalization of CK levels, he was re-challenged with brand-name atorvastatin (Lipitor) 10 mg/d without further complaints of myalgia or high CK levels (Table 1).

DISCUSSION

This individual had clinical and biochemical findings suggestive of statin-induced myopathy. During assessment of statin-induced myopathy, it is imperative first to exclude common causes of high CK levels, as well as predisposing factors for statin myopathy.³ His hypothyroidism and vitamin D deficiency were well controlled. History negative for alcohol intake or changes in exercise regimen was also reassuring. He had no prior personal or family history of myopathy.

He was also assessed for potential drug interactions predisposing to statin-induced myopathy. Elderly adults are often exposed to polypharmacy, which may increase the risk of drug-drug interactions.² The prevalence of potential drug–drug interactions increases with the number