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BRIEF COMMUNICATION

Explicit memory training leads to improved memory for face–name pairs in patients with mild cognitive impairment: Results of a pilot investigation

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Abstract

Relatively few studies have examined the use of cognitive rehabilitation in patients with mild cognitive impairment (MCI), largely due to the assumption that training will not improve functioning in patients with progressive conditions. Face-name association, an ecologically valid task, is both dependent on the explicit memory system and difficult for MCI patients. During three hour-long sessions, eight patients diagnosed with MCI were trained in the use of explicit memory strategies with 45 face-name pairs. For each pair, they were taught to visually identify a facial feature, link a phonological cue to that feature, and recall the associated name. There was significant improvement in recognition accuracy, along with faster reaction times, for trained face-name pairs. Improved accuracy persisted when tested one month after training. Significant, but less, improvement was also found on untrained stimuli, raising the possibility of generalization of training strategies. Preliminary results suggest strategy-based cognitive rehabilitation may be beneficial in patients with MCI, though these results must be replicated with a control group to rule out practice effects. (*JINS*, 2008, *14*, 883–889.)

Keywords: Cognitive rehabilitation, Alzheimer's disease, Dementia, Aging, Associative memory, Multi-domain MCI

INTRODUCTION

The benefits of explicit memory training (EMT) are recognized for patients with traumatic brain injury (TBI) (Cicerone et al., 2005; NIH, 1998); however, little research has investigated EMT in patients with progressive illnesses such as Alzheimer's disease (AD). Despite some evidence that EMT is beneficial in early AD (Acevedo & Loewenstein, 2007; De Vreese et al., 2001), Clare and Woods (2004) concluded that such training is not strongly supported in this population, presumably due to their severe explicit memory impairments.

Mild cognitive impairment (MCI) is often a transitional stage between normal aging and AD (Petersen, 2004). The period of relatively preserved memory functioning after initial diagnosis of MCI but before progression to AD (Smith et al., 2007), may be due to compensatory mechanisms observed in functional neuroimaging studies (Dickerson et al., 2005). This period presents an opportunity to intervene with strategies to maximize memory functioning and possibly delay further decline.

The few studies of EMT in patients with MCI yielded discouraging results. Rapp et al. (2002) found no objective evidence of improvement in patients with MCI and Belleville et al. (2006) found only limited improvement after training. Similarly, EMT was ineffective in older adults with below average memory functioning (Unverzagt et al., 2007). However, these studies taught patients varied mnemonic strat-

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egies that made it difficult for them to select and use the appropriate strategy during posttraining memory testing (Rapp et al., 2002). Thus, training a single mnemonic strategy that can be applied to multiple types of information may be more beneficial than training with multiple strategies (Stringer, 2007).

Face-name association offers an ecologically valid learning and memory task that is difficult for patients with MCI (Petrella et al., 2006) and AD (Sperling et al., 2003) and is associated with the explicit memory system (Sperling et al., 2001). Importantly, the brain regions within this system are the most severely affected during progression from MCI to AD (Whitwell et al., 2007). Following EMT, Belleville et al. (2006) found significant improvement on a face-name task in MCI patients. Within the AD literature, EMT for face-name associations has ranged from ineffective (Backman et al., 1991; Metzler-Baddeley & Snowden, 2005) to significantly beneficial, with improvements persisting at 3- and 6-month follow-up assessments (Acevedo & Loewenstein, 2007).

We report here on the use of a novel EMT paradigm in patients with MCI. We used a face-name association task that was based on the Biographical Information Module of the Ecologically Oriented Neurorehabilitation of Memory (EON-Mem) program (Stringer, 2007), which is clinically effective in TBI and stroke patients, but has not previously been applied to MCI. This pilot study was conducted in conjunction with a functional magnetic resonance imaging (fMRI) study, which revealed increased activation in neocortical areas associated with memory (Hampstead et al., 2008). As cognitive rehabilitation is not routinely offered to MCI patients, the majority of whom are expected to decline toward AD, and because previous studies of cognitive rehabilitation in MCI have been mostly negative, we believe it is important to alert both clinicians and researchers to novel and potentially efficacious interventions, even at the pilot stage.

METHODS

Participants

The study was approved by the Institutional Review Boards of Emory University and the Atlanta Veterans Affairs Medical Center (VAMC). Eight Caucasian patients gave informed consent and were recruited from the Emory University Alzheimer's Disease Research Center and the Atlanta VAMC. All were diagnosed with amnestic, multi-domain MCI (Petersen, 2004) during a consensus conference based on neurological, neuropsychological, laboratory, and neuroimaging findings. Activities of daily living (ADLs) and instrumental ADLs were reported as intact at the time of participation by both the patient and a family member, thereby ruling out a diagnosis of dementia. Six of the patients completed the Dementia Rating Scale-2 (DRS-2, Jurica et al., 2001) and the Geriatric Depression Scale (Yesavage et al., 1982–1983) during the first session to briefly reassess their cognitive functioning at the time of study participation. Although two patients performed fully within normal limits on the DRS-2, they demonstrated deficits during the more comprehensive evaluation as noted above, suggesting the DRS-2 was not sufficiently sensitive to detect their impairments. Demographics and test performances for all subjects are given in Table 1.

Stimuli

Ninety faces were selected from the Kirwan and Stark (2004) face set, transformed to grayscale images, and divided into two lists of 45, matched for gender, race, and approximate age (by decade). Each face was randomly paired with a gender-appropriate name from one of two lists matched for length (5–6 letters) and popularity by decade.

Procedures

Each patient completed pre- and posttraining assessments and three training sessions over the course of 2 weeks. The posttraining assessment always occurred 2 days after the third training session. During the assessment sessions, patients were exposed to all 90 novel face-name pairs in blocks of five, where each pair was presented for 5 seconds with a 1-second inter-stimulus interval. Patients were instructed to remember the face-name associations; no overt response was required. These active blocks alternated with 20-second rest blocks when patients stared at a fixation cross. The six subjects participating in the fMRI study (Hampstead et al., 2008) saw these stimuli during scanning, the other two viewed them on a computer screen in a quiet room. Fifteen minutes after seeing the last face-name pair, patients completed a four-alternative recognition memory test involving all 90 pairs. The four choices used in this test were the target name, a foil from the list used in training, a foil from the untrained list, and a novel foil. This test design reduced chance level performance to 25% and also varied foil familiarity.

Patients underwent three face-name training sessions, with an average of 2.8 days ($SD = 0.8$) in between. Patients were assigned one of the two lists of 45 pairs, in counterbalanced order. Training used a modified Biographical Information Module from the EON-Mem program (Stringer, 2007). Although this module teaches patients to self-generate cues to facilitate learning and memory, we provided these cues to standardize procedures across subjects. For each face-name pair, patients were directed to a salient facial feature (visual cue) and were given a "nickname" (verbal cue) linking the facial feature to the name. Verbal cues were phonologically similar to, and typically rhymed with the actual name. Examples of the faces and cues can be seen in Figure 1. Patients were instructed to associate the visual and verbal cues in detailed mental images that exaggerated and emphasized the salient facial features. On each subsequent training trial, patients were required to first recall the visual cue, then the verbal cue, and finally the corresponding name.

Table 1. Demographics, average trials needed during training, and memory performance of patients

Sex	Age	Education	DRS-2 AEMSS	DRS-2 Memory (SS)	DRS-2 Attention (SS)	DRS-2 I/P (SS)	DRS-2 Construct (SS)	DRS-2 Concept (SS)	GDS	Average Trials Needed	Percent Improvement–Trained List	Percent Improvement–Untrained List
M	73	12	—	—	—	—	—	—	—	27.9	31.1	8.9
F	86	16	—	—	—	—	—	—	—	21	40.0	15.6
F	73	15	5.8	2	11	12	10	10	3	43.4	26.7	11.1
M	79	14	3.9	5	12	3	10	8	1	25.2	46.7	6.7
M	72	16	10	6	11	12	10	13	0	19.9	68.9	20.0
M	63	16	8.9	10	11	11	10	9	4	16.3	64.4	31.1
F	75	15	10.3	10	12	10	10	12	0	15.9	60.0	28.9
M	79	18	3.8	4	10	5	10	9	2	28.9	44.4	0
Mean	75	15.3	7.1	6.2	11.17	8.8	10	10.2	1.7	24.8	47.78	15.28
(SD)	(6.7)	(1.8)	(3)	(3.3)	(.75)	(3.9)	(0)	(1.9)	(1.6)	(9.0)	(15.44)	(10.85)

Note. The number of trials possible during training ranged from 15 (best)–50 (worst). Percent improvement on the trained and untrained lists were calculated by subtracting pre-training memory test accuracy from post-training accuracy. DRS-2 and GDS were collected during session 1; DRS-2 = Dementia Rating Scale-2; AEMSS = Age and education-matched scaled score; I/P = Initiation/Perseveration index; Construct = Construction index; Concept = Conceptualization index; SS = scaled score; GDS = Geriatric Depression Scale.

During each training session, patients were trained on 15 face-name pairs, in three successive groups of five. For each pair, they were required to spontaneously recall the name on three consecutive trials, with a maximum of 10 trials to reach this criterion. Following completion of the third group of five pairs, all 15 pairs were reviewed as a single group, with three trials for each pair (same day review). The next training session began with a review of all 15 pairs trained during the previous session, again with three trials for each pair (delayed review).

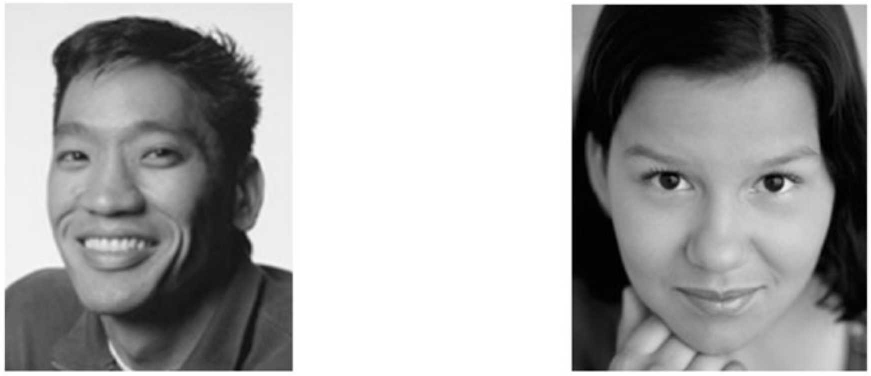
Six patients returned for a 1-month follow-up, during which they again completed the face-name test and were asked to make memory confidence ratings for each trial using a 4-point scale (1 = not confident at all, 4 = extremely confident). Importantly, they had not been exposed to any of the face-name stimuli during the 1-month interval. Two patients were unable to return at follow-up for logistical reasons but were similar to the remainder of the patients on all variables in Table 1.

RESULTS

Memory Test Performance

Recognition accuracy (Figure 2a) was assessed using a 2 × 2 repeated-measures analysis of variance (ANOVA) with factors of list (trained, untrained) and time (baseline, post-training). There was a significant main effect of list [$F(1,7) = 59.7$; $p < .001$; partial $\eta^2 = .9$], indicating significantly better performance on the trained list. The main effect of time was significant [$F(1,7) = 54.9$; $p < .001$; partial $\eta^2 = .89$], as was the list-by-time interaction [$F(1,7) = 63.8$; $p < .001$; $\eta^2 = .9$]. This interaction arose because performance was similar between lists at baseline ($t_{14} = 1.5$; $p = .15$) but was greater posttraining for the trained compared with the untrained list ($t_{14} = 5.4$; $p < .001$). There were, however, significant improvements for both trained ($t_7 = 8.8$; $p < .001$) and untrained lists ($t_7 = 4.0$; $p = .005$) relative to baseline. The correlation between general memory functioning [DRS-2 Memory scaled score (SS)] and improvement after training was nearly significant for the trained list ($r = .8$; $p = .057$) and significant for the untrained list ($r = .85$; $p = .03$).

Response latencies (Figure 2b) revealed a significant main effect of list [$F(1,7) = 7.7$; $p = .03$; partial $\eta^2 = .52$], indicating that patients made faster responses for trained pairs compared with untrained pairs. There was no main effect of time [$F(1,7) = 0.6$; $p = .48$; partial $\eta^2 = .07$] but there was a significant list-by-time interaction [$F(1,7) = 8.7$; $p = .02$; partial $\eta^2 = .55$], reflecting similar response times at baseline ($t_{14} = 0.2$; $p = .84$) but faster posttraining responses for the trained compared with the untrained list ($t_{14} = 2.45$; $p = .03$). General memory functioning (DRS-2 Memory SS) showed no correlation with the change in response latency (trained: $r = .05$; $p = .9$; untrained: $r = -.31$; $p = .55$).



SHAWN
Visual cue: Large mouth that opens wide to yawn
Verbal cue: "Yawn"

RACHEL
Visual cue: Smooth, clear skin, like she had a facial
Verbal cue: "Facial"

Fig. 1. Examples of the stimuli and cues used during training.

One-Month Follow-up

Patients demonstrated a slight but nonsignificant decline in accuracy on the trained list compared with posttraining (t_5 = 2.2; p = .08), but performance remained significantly above baseline (t_5 = 5.7; p = .002). Patients were significantly slower to respond to pairs from the trained list compared with both baseline (t_5 = 3.7; p = .01) and posttraining (t_5 = 3.7; p = .01). Recognition accuracy on the untrained list declined significantly from posttraining levels (t_5 = 3.1; p = .03) and was similar to baseline performance (t_5 = 0.7; p = .54). Patients were slower to respond compared with baseline (t_5 = 2.8; p = .04) but this difference was not significant compared with posttraining (t_5 = 1.9; p = .12). Additionally, patients were significantly more confident in selecting the correct names for the trained compared with the untrained list (t_{10} = 2.5; p = .03).

Use of Cues During Training

Overall, patients required an average of 24.8 trials (SD = 9.0) to reach criterion during training (possible range: 15–50). There was a significant inverse correlation between the number of training trials needed to reach criterion and the DRS-2 Memory SS ($r = -.91$; p = .01). There was also a significant inverse correlation between the average number of trials needed to reach criterion and the improvement on the trained list ($r = -.81$; p = .02) that persisted even when the most severely impaired patient (patient 3) was excluded from analysis ($r = -.76$; p = .048). There was no correlation between the number of training trials and improved response latency for the trained list ($r = -.34$; p = .42).

Patients were able to remember both the visual and the verbal cue on the majority of trials during the same day and delayed reviews. A 2 $\times$ 2 ANOVA with factors of cue type and time suggested that patients remembered the visual cues better than the verbal cues, although the main effect of cue type fell just short of significance [$F(1,7)$ = 5.3; p = .056; partial η^2 = .43]. There was a significant main effect of time, such that patients recalled fewer cues between training sessions [$F(1,7)$ = 6.1; p = .04; partial η^2 = .47). The cue-by-time interaction was not significant [$F(1,7)$ = 4.5; p = .07; partial η^2 = .39]. Recollection of both visual (r = .81; $p < .001$) and verbal cues (r = .94; $p < .001$) was significantly correlated with spontaneous recall of names during the review trials.

DISCUSSION

The current study shows that EMT techniques may be quite effective in patients with MCI. Specifically, our patients demonstrated 27–69% improvement in recognition accuracy for the trained face-name pairs after only three hour-long training sessions. Significant improvement remained evident 1 month after training. From a psychosocial standpoint, the improved accuracy, faster responding, and increased confidence for the trained pairs could help patients avoid uncomfortable social interactions that come with difficulty remembering names. The specificity of the behavioral effects, as well as associated increases in fMRI activation in regions implicated in explicit memory that were unique to the trained stimuli (Hampstead et al., 2008), suggests that these changes were induced by the training provided. Additionally, the strong relationship between baseline memory functioning and behavioral improvement suggests that earlier intervention in this population could lead to greater benefit.

Our results support previous studies suggesting that EMT can be effective in MCI and AD (Acevedo & Loewenstein, 2007; Belleville et al., 2006; Loewenstein et al., 2004). Importantly, our patients showed substantial improvement after learning approximately 4 times the number of face-name pairs used in these other studies. This magnitude of improvement may be attributed to the highly focused nature of our intervention, whereas the variety of mnemonic strategies used in a previous study may have been overwhelm-

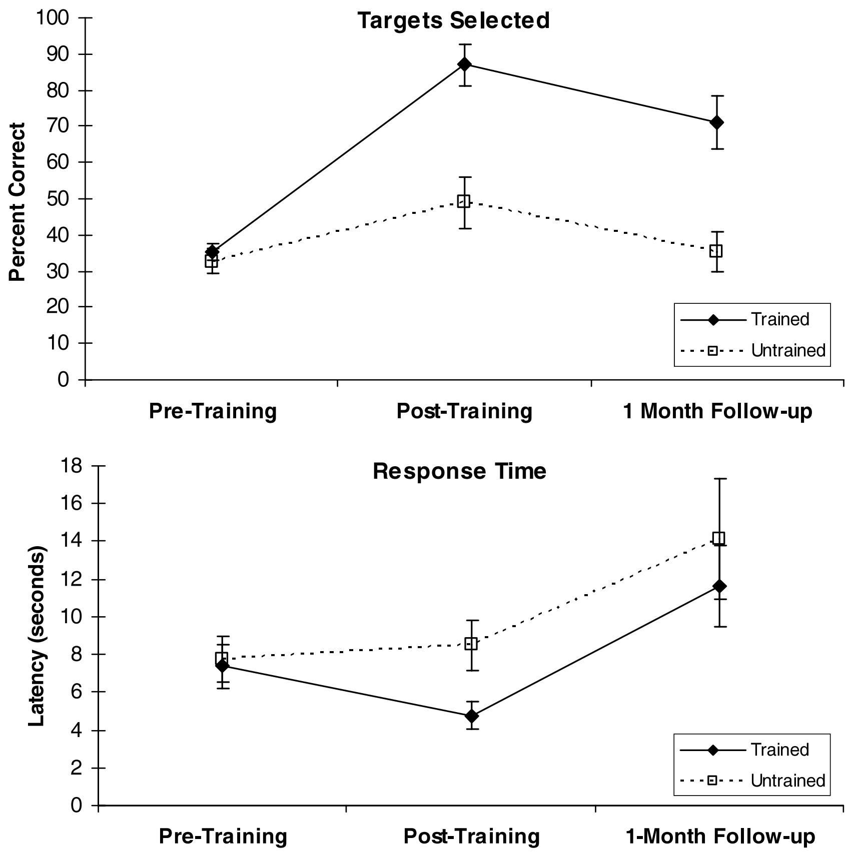


Fig. 2. Mean recognition accuracy (a) and median response time (b) on the memory test at each time point. Error bars represent *SEM*.

ing and thus counterproductive to patients (Rapp et al., 2002). Our strategic use of verbal cues that rhymed with the name may have facilitated recognition accuracy since rhyming has been shown to improve memory (e.g., Gupta et al., 2005). Future studies could directly contrast single and multiple mnemonic strategy approaches in their ability to improve memory performance.

It is possible that factors such as repeated exposure to the stimuli, or the specific cues provided, could have contributed to the observed improvements. Although we cannot fully rule out such factors at this time, two pieces of evidence suggest that the observed improvements on the trained list are attributable to use of the strategies. First, there was a significant inverse correlation between the number of training trials needed to reach criterion and improved memory for the trained stimuli; a positive correlation would be expected if the amount of exposure to the stimuli determined behavioral improvement. Second, there were significant correlations between spontaneous name recall and recollection of both visual and verbal cues during the review periods. Inclusion of an independent control group in future studies would further address the extent to which improved memory test performance is due to the trained strategies.

We provided patients with the cues for each face-name pair during training to standardize the procedures; however, real-world utility of the strategies depends on the ability to spontaneously generate cues. In this respect, the significant posttraining improvements on the untrained list are encouraging, especially considering that all our patients anecdotally reported attempting to use the strategies during the posttraining exposure. Previous studies in healthy older adults that have used task-specific training have shown generalization to similar tasks (West et al., 2000). We cannot rule out the possibility that practice effects contributed to improvement on the untrained list, especially considering that performance returned to baseline after 1 month. However, the brief exposure time (5 s), the large number of pairs used, and the 2-week period between baseline and posttraining memory testing suggest that practice effects alone are unlikely to account for the improvements seen on the untrained stimuli. Nonetheless, future studies could address these concerns by including novel stimuli during the posttraining exposure and by comparing the effectiveness of self- *versus* experimenter-generated cues.

Although our pilot study had a small sample size, memory training must be effective on an individual level: our large effect sizes are evidence of this efficacy. Including a test of free recall may provide a more accurate measure of the ecological validity of training. Our results should be replicated with an independent control group to rule out practice effects. Despite these limitations, our preliminary results provide support for the efficacy of one EMT technique (visual-verbal cueing for face-name associations) in patients with MCI. These findings are especially encouraging given the relative paucity of research investigating memory rehabilitation for patients with MCI and early AD. Future randomized control trials with larger sample sizes are needed to confirm our pilot results, explore the use of other EON-Mem Modules in MCI and AD, and study generalization of treatment effects to real-world situations.

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