

Original Research Article

A Pilot Study of Training and Compensation Interventions for Mild Cognitive Impairment

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Key Words

Rehabilitation · Memory · Geriatric patients · Feasibility · Adherence · Effect size · Pilot clinical trial

Abstract

Background: This pilot clinical trial sought to estimate the feasibility and efficacy of two interventions aimed at improving memory performance in geriatric clinic patients with mild cognitive impairment. **Methods:** Fifteen participants were randomized to either a memory training group or a memory compensation group. **Results:** Recruitment rates were low, whereas adherence and retention rates were acceptable. The memory training group improved in self-reported memory abilities and satisfaction with memory. The memory compensation group improved on one objective memory test but showed no consistent changes on any other outcomes. **Conclusion:** Effect size estimates will inform the design of larger clinical trials.

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Introduction

Mild cognitive impairment (MCI) is characterized by the presence of subjective memory complaints and cognitive impairment demonstrated on objective testing, when the breadth and depth of impairment and its functional impact do not meet the criteria for dementia [1]. Recent studies demonstrating learning and cognitive plasticity in individuals with MCI [2, 3] have propelled an increased interest in cognitively based interventions for this population [4–6]. In older adults *without* cognitive impairment, memory training improves both objective and subjectively measured memory functioning, and it may contribute to the mainte-

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nance of functional independence through improvement of basic memory abilities [7–11]. Unfortunately, the efficacy of cognitive interventions in patients with amnesic MCI is less well established. Participants in the population-based ACTIVE trial whose memory test performance was impaired at baseline did not benefit from memory training [12]. Early studies on participants with memory impairment showed some benefit from memory and cognitive training but did not use systematic criteria for the diagnosis of MCI, or did not target this population selectively [13–15].

A recent systematic review of the literature examined effect sizes in 15 studies of cognitive interventions in formally diagnosed patients with MCI. Significant improvements were observed on 44% of objective measures of memory and 12% of self-report measures of memory, quality of life or mood/anxiety [16]. Individual components of the interventions varied widely across the studies: all interventions targeted memory specifically, with some also aimed at other cognitive abilities such as executive functioning or language. Eleven of the 15 studies (73%) involved training in mnemonic strategies that target the ability to process, store, and retrieve new information (memory training). An additional 3 studies used memory training in combination with compensatory strategies. Compensatory strategies to rehabilitation are approaches that circumvent memory impairment by instructing the individual in the use of external aids, such as calendars, timers or agendas (memory compensation) [17]. Only one study used an intervention based solely on memory compensation rather than memory training.

With progression to dementia, there is a successive decline in an individual's ability to engage in the cognitively demanding strategies that are taught in memory training approaches. However, procedural memory is relatively spared; thus, the effects of cognitive intervention might be longer-lasting if they focused on teaching procedures to compensate for memory impairment. Instruction in the use of external memory aids, with its focus on schedules and to-do lists, might also be more likely to result in improved outcomes in terms of everyday functional abilities. To date, only one study has focused on the development of purely compensatory strategies for improving memory functioning, showing improvements in mood, self-efficacy, and self-reported functional abilities in patients with MCI who were taught to use external memory aids [18].

With these considerations in mind, we designed a randomized clinical pilot study to evaluate the feasibility and efficacy of two different cognitive interventions delivered over seven weekly sessions in patients with MCI. The design included two active treatment arms, and a wait-listed, no-contact, control group. Both active treatment groups included a psycho-education component; however, the memory training group received training in mnemonic strategies, whereas the memory compensation group received training in procedures for using an agenda as an external memory aid. We predicted that (1) the memory training group would improve on objective memory tests that rely on successful use of the trained strategies; (2) the memory compensation group would not improve on objective memory tests but would improve on self-report measures of everyday memory functioning, and (3) that both active treatment groups would improve on ratings of satisfaction with memory.

Methods

Participants

English-speaking persons with a diagnosis of MCI were recruited amongst eligible patients attending the outpatient geriatric assessment clinics of McGill University Health Centre. To identify eligible patients, referring clinicians reviewed all clinical data, including any tests administered within the 6 months preceding enrollment. MCI was diagnosed in a

clinical team conference and defined by the following features: (1) a clinical history of progressive decline in memory reported by the patient and/or an informant (e.g. a family member or health care professional); (2) objective cognitive impairment without dementia (a Montreal Cognitive Assessment test score $<26/30$, with a Mini-Mental Status Exam score $\geq 24/30$); (3) mild or no impairment in instrumental activities of daily living (as per clinical interview, Barthel Index and OARS IADLS scale), and (4) an absence of gross abnormality on brain CT scan sufficient to account for cognitive impairment. The diagnosis and subtypes of MCI were confirmed during baseline neuropsychological testing. Patients deemed unable to comply with the treatment program due to a significant comorbid illness or an anticipated inability to attend all study sessions were excluded. Study recruitment occurred in three waves to coincide with three offerings of the interventions (fall 2008, spring 2009, fall 2009).

Randomization and Blinding

After providing informed consent and attending a baseline assessment visit, the participants were randomly assigned to one of the three groups: memory training, memory compensation, or wait-list control. The participants could not be blinded to the treatment condition, but they were naive regarding the specific hypotheses associated with the two active treatment arms. The neuropsychologist (L.K.) who obtained the objective outcome measures was blind to the group assignment. In the third wave of recruitment, all participants were randomized to one of the two active treatment groups to maximize the data obtained from these interventions.

Interventions

The active treatment programs consisted of seven 90-min weekly training sessions as well as a schedule of homework assignments for practicing the skills taught in each session. The active treatment groups ran concurrently with regularly scheduled weekly sessions. Treatment was administered to groups of 2–3 participants by a registered clinical neuropsychologist (J.C.). The two active interventions were based on principles of effective learning as developed and tested in cognitive psychology and clinical neuropsychology [19, 20]. Learning was facilitated through the use of meaningful or elaborative rehearsal, the method of vanishing cues, distributed practice (homework exercises to supplement in-session practice), over-learning, and spaced retrieval. Homework focused on the practice of the mnemonic strategies in a workbook and applying the strategies to specific real-world situations.

Session 1 in both interventions began with a psychoeducational component, covering the structure of memory, its development across the lifespan, emotional and functional impacts of cognitive impairment, beliefs about memory and their impact, and factors influencing cognition such as anxiety, fatigue, diet, and exercise. Table 1 shows the specific skills taught in sessions 1–7 for each intervention. Session 7 consisted of a review of all concepts and procedures.

Memory Training Intervention

The memory training intervention was adapted from the MEMO approach used at the Institut Universitaire de Gériatrie de Montréal and described in detail elsewhere [15], following the participation in a 2-day intensive training workshop by two investigators (J.C. and L.K.). In brief, the participants were first given training in selective attention and visual imagery skills, and then learned how to apply these skills to mnemonic strategies that support new learning in different contexts.

Table 1. Content of sessions 1–7 for each intervention group

Session	Memory training intervention	Memory compensation intervention
1	<ul style="list-style-type: none"> – Psychoeducation – Introduction to principle of overcoming memory decline 	<ul style="list-style-type: none"> – Psychoeducation – Moving the Today marker – Logging daily activities
2	<ul style="list-style-type: none"> – Impact of attention on memory – Training in selective attention skills 	<ul style="list-style-type: none"> – Introduce Monday through Sunday sections, permanent schedule page, log page, Things to Do section – Training in Cross, Notation and Note procedure for logging activities
3	<ul style="list-style-type: none"> – Training in visual imagery 	<ul style="list-style-type: none"> – Training in procedures for adding, canceling, and changing events – Sunday Night Procedures for review and planning
4	<ul style="list-style-type: none"> – Method of loci for learning words 	<ul style="list-style-type: none"> – Training in use of Calendar section – Training in use of Last-Week section – Further rehearsal of Sunday Night Procedures
5	<ul style="list-style-type: none"> – Semantic elaboration and association to support learning of face-name associations 	<ul style="list-style-type: none"> – Training in use of Address Book – Begin transfers into Address Book – Begin transfer of important dates into Calendar section
6	<ul style="list-style-type: none"> – PRST method to support learning of text information 	<ul style="list-style-type: none"> – Train to log activities at 3 specific times each day – Introduction to Archive section – Introduction to special sections for important names and current medications – Complete transfer of medication list, addresses, and calendar dates
7	<ul style="list-style-type: none"> – Review 	<ul style="list-style-type: none"> – Review and troubleshooting

PRST = Preview, Question, Read, State, Test.

Memory Compensation Intervention

The memory compensation intervention is a novel set of procedures adapted from approaches used for promoting independent living in amnesic individuals. It draws on principles of effective training in organizational strategies and procedural learning to assist participants with setting up an external memory support system and integrating it into everyday life. Practice in both treatment sessions and real-world situations is included to ensure the effective use of the memory book [21]. Homework is designed to gradually increase the use of the agenda across a range of everyday situations. In session 1, the participants were given a paper agenda, taught how to log daily activities for the next week, and instructed to record every activity they engaged in. This record was used in session 2 to create a permanent, individualized schedule that included routine daily activities. Subsequent sessions focused on learning to use various features of the agenda including a permanent calendar and schedules, log pages, Things to Do, Address Book, and special sections for recording medications and important names (table 1). All procedures were rehearsed in-session using the method of vanishing cues. Every session began with a review of all procedures learned to date, and homework based on the new procedures was checked to provide the participants with feedback and address any difficulties that arose with completing the procedures.

Wait-List Control

The wait-list control group underwent repeated assessments over the same time interval as the active treatment groups but did not receive any other intervention during that period. Six months later, these individuals were re-tested and then re-randomized to one of the active treatment groups with a subsequent cohort of participants.

Data Collection Procedures and Outcome Measures

Data on age, sex, years of formal education, preferred language, current medications, and scores on clinical screening tests were obtained from patient charts. Attendance rates, completion and correctness of homework assignments were recorded by the treating neuropsychologist (J.C.) to evaluate adherence to the intervention programs. Pre- and postintervention assessments took place within 2 weeks of the start and end of the intervention. The order of alternate forms of tests (used to eliminate content-specific practice effects) was counterbalanced across participants in each group. Repeated assessments in the wait-list control group coincided with those of the intervention groups.

Effects of intervention on objective measures of memory performance were measured using experimental tests, in which the stimuli were exposed for a longer duration than in traditional neuropsychological tests to allow the participants sufficient time to employ strategies for encoding the material [15]. The tests involved a visual presentation for 3 min followed by immediate recall of: (1) a short-story text; (2) 12 faces paired with last names, and (3) a 12-item word list. Delayed recall of the 12-item word list was assessed after a 10-min interval filled with other cognitive testing. Effects of intervention on patient-reported memory outcomes were assessed with the Multifactorial Memory Questionnaire's Ability, Strategy Use, and Contentment scales [22]. Indirect effects of the cognitive interventions were examined with the Rivermead Behavioural Memory Test and standardized nonmemory neuropsychological tests including FAS and Animals tests of verbal fluency, the Victoria Stroop Test of executive control, and the Digit Span Forward (attention) and Backward (working memory).

Statistical Analyses

Baseline characteristics of the three groups were compared using independent t tests and χ^2 tests. Primary analyses involved an evaluation of recruitment, retention and adherence rates, as well as separate estimates of raw and standardized effect sizes (with 90% confidence intervals) on the primary and secondary outcomes for each group.

Results

Eligibility and Recruitment

Of the 50 individuals identified as eligible for participation in the study by referring clinicians, 8 were unable to be contacted, 18 indicated they were not interested, 5 indicated they were too busy, and 1 individual had passed away prior to being contacted. Thus, the 18 remaining eligible patients were enrolled in the study and randomized to the memory training (n = 10, initially 8), memory compensation (n = 8, initially 6) or wait-list control (n = 4) groups. Those initially randomized to the wait-list group were re-randomized to one of the active treatment groups with subsequent cohorts.

Withdrawals

Fifteen participants completed the pre- and postevaluations: 8 in the memory training group; 7 in the memory compensation group. Reasons for withdrawing from the memory

Table 2. Demographic and clinical characteristics and performance on baseline-only tests for the three groups

Variables	Memory training group (n = 8)	Memory compensation group (n = 7)	Wait-list control group (n = 4)
Age, years	79±8, 67–91	78±4, 73–83	77±5, 71–83
Males/females	4/4	3/4	2/2
Education, years	11±6, 4–23	12±6, 3–20	10±6, 3–16
Evidence of cardiovascular disease ^a	3 (out of 6)	3 (out of 6)	2 (out of 3)
Mini-Mental Status Exam ^b	27±3, 23–30	27±2, 23–30	26±2, 23–27
Montreal Cognitive Assessment ^b	20±5, 9–25	21±2, 18–25	22±2, 19–24
MCI subtype			
Amnestic single domain	1	2	1
Amnestic multidomain	4	4	2
Nonamnestic single domain	2	1	1
Nonamnestic multidomain	1	0	0
Boston Naming Test ^d	7±3, 2–11	8±3, 5–13	8±4, 3–13
WAIS-III Vocabulary ^d	9±4, 5–17	11±3, 8–15	8±1, 8–9
Digit Span Forward (max.) ^e	–0.3±1.2, –1.6 to 1.9	0.2±0.9, –0.8 to 1.5	0.5±1.2, –0.7 to 2.1
Rey Complex Figure Copy	22±6, 14–31	16±9, 7–28	21±10, 7–28
Stroop Interference ^d	–0.2±1.0, –1.7 to 1.0	–0.5±1.3, –2.9 to 0.7	–1.1±2.3, –4.2 to 1.0
Barthel Index	97±5, 85–100	100±0	100±0
OARS	12±3, 6–14	13±2, 10–14	14±0
Geriatric Depression Scale ^c	3±2, 1–7	2±2, 0–6	3±1, 2–3

The descriptive statistics shown include only participants who completed the study. Where appropriate, values are given as mean ± SD, range.

^a As indicated by CT scan results where available; ^b maximum score = 30; ^c maximum score = 15; ^d the scores shown are age-corrected, scaled scores; ^e the scores shown are age-corrected z-scores.

training group included: no longer wanting to participate (n = 1) and hearing loss that caused difficulty in following the intervention sessions (n = 1). The reason for withdrawal from the memory compensation group was dissatisfaction at not being taught memory training strategies (n = 1).

Effectiveness of Randomization

Table 2 presents the characteristics of the participants who completed the study. Data for the memory compensation group includes 2 individuals who are also in the wait-list control group. Participants were well distributed across the three groups in terms of age, sex, and years of formal education. They had similar distributions of MCI subtypes and performed similarly on baseline assessments of global cognitive functioning and mood. Four participants scored between 5 and 10 points on the Geriatric Depression Scale, suggesting mild depressive symptoms, and 8 participants had evidence of cerebrovascular disease as indicated by CT scans showing microvascular disease or mild ischemic changes.

Adherence

Table 3 shows the results for adherence to the active interventions. On average, in comparison to the memory training group, participants in the memory compensation group attended fewer training sessions (5.4 vs. 6.9), completed fewer assignments (9.9 vs. 10.3), and were less likely to complete homework assignments correctly (6.7 vs. 7.8); however, these differences were not significant.

Table 3. Number of sessions attended, homework assignments completed, and correctness of homework for the intervention groups

Intervention	Attendance	Homework	
		compliance	correctness
Memory training	6.9±0.4	10.3±2.2	7.8±3.5
Memory compensation	5.4±1.8	9.9±1.9	6.7±2.3

Values are given as mean ± SD. Total number of sessions = 7; maximum compliance score = 12; maximum correctness score = 12. Participants were considered noncompliant if they attended <6/8 sessions or completed <6/8 homework assignments.

Efficacy

Table 4 shows the mean changes of scores, effect sizes with 90% confidence intervals, and p values of objective and patient-reported measures of cognitive functioning in the three groups. Overall, no group-level changes were observed in objectively measured memory performance in response to either intervention. One exception was an unexpected improvement in delayed recall of the word list amongst the memory compensation group participants (effect size: 0.59, p = 0.03). A significant improvement in self-reported memory ability was observed in the memory training group (effect size: 0.86, p = 0.02), which also tended to show improvements in self-reported contentment with memory (effect size: 1.1, p = 0.06) and strategy use (effect size: 0.76, p = 0.16). Weaker, nonsignificant improvements in self-reported memory ability and contentment were observed in the memory compensation group (both effect sizes: 0.46, p > 0.05). No significant changes were observed in any of the groups on the Rivermead Behavioural Memory Test, nor on more distal measures of cognitive functions including attention, verbal fluency, working memory, and executive control.

Discussion

The aims of the current pilot study were to examine the feasibility, acceptability, adherence rates, and efficacy of two cognitive intervention protocols for patients with MCI recruited from the geriatric outpatient clinics of a university-based hospital.

To ensure that all participants had undergone comprehensive geriatric assessment and met the criteria for MCI, recruitment for this study was limited to a population of 50 eligible patients within the McGill University Health Centre's Geriatrics Division. Initial recruitment rates were unexpectedly low (36% of the eligible patients). Although patients at our clinics had expressed a general need for instruction on how to maintain or improve cognitive abilities, nearly half of the individuals (46%) who met the study's inclusion criteria indicated that they were not interested or too busy to participate in the program. We note that reporting of recruitment rates in cognitive intervention studies is rare. With few exceptions [18], the recruitment strategies employed, e.g. community newspaper advertisements, tend to preclude a determination of the size of the eligible population, making it difficult to identify strategies for optimizing recruitment in future trials. Prior to beginning a larger, multicenter trial, it would be important to pinpoint the motives for not participating – whether the intervention did not appeal to the needs of the invited participants, whether it seemed intimidating or overwhelming, or even whether getting to the hospital was too complicated and the participants would be better served in a community setting.

Table 4. Effect sizes on objective and subjective measures of cognitive function by groups

Outcomes	Memory training group (n = 8)				Memory compensation group (n = 7)				Wait-list control group (n = 4)			
	mean change	ES _{std}	90% CI	p	mean change	ES _{std}	90% CI	p	mean change	ES _{std}	90% CI	p
<i>Primary</i>												
<i>Immediate memory</i>												
Visual short stories	3.13	0.18	-9.4 to 15.6	0.65	5.71	0.32	-10.1 to 21.6	0.51	7	0.39	-17.5 to 31.5	0.55
Word list – immediate	0.38	0.14	-1.4 to 2.2	0.70	-0.14	-0.05	-0.9 to 0.6	0.74	0.8	0.28	0.2 to 1.4	0.06
Face-name	0.563	0.07	-4.9 to 6.0	0.85	2.43	0.29	-2 to 6.9	0.33	-1.63	-0.20	-7.8 to 4.6	0.58
<i>Delayed memory</i>												
Word list – delayed recall	0.25	0.07	-1.6 to 2.1	0.81	2.17	0.59	0.7 to 3.7	0.03*	0.5	0.14	-1.5 to 2.5	0.60
<i>Self-reported memory</i>												
MMQ – Ability	10.9	0.86	4.0 to 17.8	0.02*	5.8	0.46	-5.1 to 16.7	0.34	6.8	0.53	-7.0 to 20.6	0.33
<i>Secondary</i>												
<i>Behavioural memory</i>												
Rivermead	0.25	0.05	-2.8 to 3.3	0.88	-0.57	-0.12	-3.8 to 2.6	0.74	-0.8	-0.16	-4.4 to 2.8	0.64
<i>Attention span</i>												
Digit Span Forward	0.25	0.11	-0.5 to 1.0	0.56	-0.571	-0.26	-2.4 to 1.3	0.57	-1	-0.45	-3.5 to 1.5	0.42
<i>Working memory</i>												
Digit Span Backward	0.625	0.32	-0.3 to 1.6	0.25	0	0.00	n.a.	1.00	0.25	0.13	-2.6 to 3.1	0.85
<i>Phonemic fluency</i>												
FAS test	3.5	0.27	-0.8 to 7.8	0.17	-0.286	-0.02	-0.3 to 3.3	0.86	-1.75	-0.14	-9.2 to 5.7	0.62
<i>Semantic fluency</i>												
Animals test	-1.25	-0.27	-3.6 to 1.1	0.34	-0.571	-0.12	-3.8 to 2.6	0.74	2.25	0.48	0.2 to 4.3	0.08
<i>Selective attention</i>												
Stroop effect	-0.188	-0.13	-0.5 to 0.9	0.62	0.324	0.22	-1.5 to 0.8	0.61	-1.431	-0.99	-0.4 to 3.2	0.16
<i>Patient reported</i>												
MMQ – Contentment	11.8	1.10	0.8 to 21.8	0.06	4.86	0.46	-2.5 to 12.2	0.24	1.7	0.16	-4.4 to 7.8	0.56
MMQ – Strategy Use	5.2	0.76	-1.2 to 12.4	0.16	1.71	0.23	-6.0 to 9.4	0.68	-2.3	-0.31	-6.3 to 1.7	0.27

Standardized effect sizes were calculated by dividing the mean changes of scores by the preintervention pooled standard deviations for each intervention group. ES_{std} = Standardized effect sizes; 90% CI = 90% confidence intervals; n.a. = not applicable; MMQ = Multifactorial Memory Questionnaire; Rivermead = Rivermead Behavioural Memory Test.

* = Significant, p < 0.05; bold = borderline significant, p > 0.05.

The majority of the participants (>80%) who enrolled in the present study completed both pre- and postintervention assessments. Three individuals (17%) withdrew from the study prior to the postintervention assessment, citing loss of interest as the primary reason. For comparison, dropout rates in previous studies of cognitive interventions ranged from 5 to 33% [16]. Interestingly, at the point of recruitment and randomization, most participants spontaneously expressed a desire to be randomized to the memory training group over the memory compensation group. Participants in the memory training group showed a nonsignificant tendency to attend more training sessions, complete more homework, and do homework correctly, when compared with those in the memory compensation group. These observations highlight a potential difficulty of conducting clinical trials that directly compare one intervention with another. In a recent study by Greenaway et al. [18], participants reported appreciating the opportunity to receive training in the use of external memory aids; however, the alternative in that study was no training. Some knowledge of the alternative treatment arms is a prerequisite to informed consent but may influence participants' satisfaction with and adherence to the assigned intervention.

The memory training group reported better memory performance and greater contentment with their memory after intervention, but showed no change in objective memory performance either on proximal outcomes that relied on the trained memory abilities or on a more distal objective measure of everyday memory ability. Participants randomized to the memory compensation group showed smaller, nonsignificant effect sizes on self-report

measures of memory performance and contentment and a significant improvement in one of the proximal objective outcomes (delayed recall of the word list), but no improvements in any other outcomes. This finding is consistent with those of several previous cognitive intervention studies on MCI, which reported improvements in self-reported memory ability, affective symptoms, or general well-being, while failing to demonstrate improvements on performance-based cognitive tests [23–27]. At the very least, patients appear to learn the strategies taught and develop the confidence to attempt them in everyday life. If a greater sense of well-being is considered a worthwhile goal of cognitive rehabilitation, then it is essential to determine which components of an intervention are responsible for the change. Both interventions included an educational component that could conceivably contribute to a greater sense of control and self-confidence in managing memory lapses in everyday life. The effect on self-reported memory ability in the memory training group suggests that some additional elements of this form of training may be necessary to obtain benefits from intervention.

Conclusions from this study, including a direct comparison of the results between the groups, are limited by its small sample size. Nevertheless, we have demonstrated that offering a cognitive intervention to older individuals who are at risk of developing dementia is both feasible and acceptable in this population. Previous cognitive rehabilitation studies have been criticized for being underpowered to detect changes in outcomes of interest [16]. The effect sizes estimated in this study may contribute to the calculation of the required sample size for larger-scale, clinical trials with recruitment from a wider catchment area. The results have also generated testable hypotheses about the critical ingredients in cognitive interventions for memory impairment, and about their potential impact on related outcomes such as depression, anxiety, and global cognitive functioning.

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