MEMO+: Efficacy, Durability and Effect of Cognitive Training and Psychosocial Intervention in Individuals with Mild Cognitive Impairment

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BACKGROUND/OBJECTIVES: There is no consensus on the efficacy of cognitive training in persons with mild cognitive impairment (MCI) because of the paucity of well-designed randomized controlled trials. The objective was to assess the effect of memory training on the cognitive functioning of persons with MCI and its durability and to evaluate whether this effect generalizes to daily life and whether positive effects could be obtained from psychosocial intervention.

DESIGN: Single-blind randomized controlled trial.

SETTING: Research centers of the Institut Universitaire de Gériatrie de Montréal and Institut Universitaire en Santé Mentale de Québec.

PARTICIPANTS: Older adults meeting criteria for amnestic MCI (N = 145).

INTERVENTION: Participants were randomized to cognitive training, a psychosocial intervention, or a no-contact control condition. Interventions were provided in small groups in eight 2-hour sessions.

MEASUREMENT: Outcome measures were immediate and delayed composite performance memory scores, psychological health (depression, anxiety, well-being), and generalization effects of the intervention (strategy use in everyday life, difficulties in complex activities of daily living, memory complaints). Testing was administered before training and immediately, 3 months, and 6 months after training.

RESULTS: Participants in the cognitive training condition improved on the delayed composite memory score and on strategy use in everyday life. Improvement was maintained at the 3- and 6-month follow-up assessments. Participants in the psychosocial and no-contact conditions did not show any significant improvement.

CONCLUSION: Cognitive training improves the memory of persons with amnestic MCI. The effect persists over a 6-month period, and learned strategies are used in everyday life. Cognitive training is a valid way to promote cognition in MCI.

Key words: cognitive training; mild cognitive impairment; cognition; psychosocial intervention

The term mild cognitive impairment (MCI) is broadly used to describe individuals in a prodromal stage of Alzheimer’s disease (AD).¹ These individuals do not meet criteria for dementia but are mildly impaired in cognitive tasks, and many will progress to dementia.² There is considerable interest in identifying nonpharmacological interventions to slow progression. Cognitive training is increasingly being recognized as a promising and potentially crucial approach because there is evidence that being engaged in cognitively stimulating activities can protect against cognitive decline in older adults.³ Furthermore, because their impairment is mild, persons with MCI are capable of learning and applying new strategies.

A few small-scale cognitive training studies have reported positive findings in persons with MCI, and a number of reviews have concluded that it is a potentially effective method for improving cognition and postponing cognitive decline,⁴⁻¹⁰ but many studies rely on a waitlist rather than an active control as a condition of reference, do not provide information on long-term maintenance of cognitive improvements, do not report data on mood and quality of life, and lack information on whether the learned strategies transfer to real life. These issues limit...
our ability to conclude that cognitive training improves cognition in MCI and to recommend its use as a strategy to reduce cognitive decline.²⁸⁻¹¹

There has been recent interest in the potential of interventions that target noncognitive symptoms. Symptoms of anxiety and depression are frequent in individuals with MCI¹² and have been associated with risk of future decline.¹³⁻¹⁵ One study indicated good feasibility and positive changes after use of a variant of cognitive-behavioral therapy.¹⁶ Another study showed improved mood after participation in a multicomponent program that included relaxation techniques and stress management.¹⁷ but both studies included elements of cognitive training in their program and were therefore unable to determine the isolated effect of the psychosocial component in their intervention.

Our goal was to determine the effect of cognitive training in persons with MCI in a randomized controlled study that included a psychosocial intervention as an active control condition and a no-contact control condition. This design has the advantage of isolating the effects of cognitive training while providing a meaningful active control condition that allows the contribution of each intervention to mood and well-being to be examined. Thus, a secondary objective was to measure whether a psychosocial intervention can improve the psychological health of individuals with MCI. The immediate and long-term effects of the training were assessed on proximal and distal outcome measures. Finally, we examined moderators of the effect of cognitive training.

The cognitive training used was the Méthode d’Entrainement pour Mémoire Optimale (MEMO) program.¹⁸,¹⁹ The intervention focused on learning new strategies, because our goal was to optimize encoding and retrieval. Its content was based on the hypothesis that persons with MCI have difficulty actively encoding information in memory and that attentional control deficits exacerbate their memory deficits. Thus, the program provides participants with strategies that promote elaborative encoding and attentional control capacities.

Participants randomized to the cognitive training condition were expected to have a greater increase in memory scores after training than the other groups and were expected to maintain their better performance over time. The training effect was expected to be larger for the delayed than for the immediate composite memory score based on prior work.¹⁸ Participants in the psychosocial intervention group were expected to have better posttraining scores on anxiety, depression, and well-being measures than participants in the other groups. We expected generalization to everyday life for participants enrolled in cognitive training, as shown by a reduction in their level of complaint and an increase in their use of memory strategies in daily life.

METHODS

Design

The MEMO+ cognitive training study was a three-arm, single-blind, randomized, controlled trial completed in French at two sites (Montreal, Quebec City) and registered as a clinical trial with the U.S. National Institute of Health Clinical trials registry (ClinicalTrials.gov Identifier: NCT01448148). The protocol was published previously and adheres to the Consolidated Standards of Reporting statement. Participants were randomized to a memory intervention group, a psychosocial intervention group, or a no-contact control group (Figure 1). A statistician who was not involved in the project performed randomization, which was centralized (at the Institut Universitaire de Gériatrie de Montréal), using a computerized random list. Randomization was performed according to site and waves of 12 to 15 participants. There were one preintervention (PRE) and three postintervention assessments (1 week (POST), 3 months (POST3), and 6 months (POST6) after the end of training). Training was provided over a 2-month period. A booster session was offered approximately 1 week after POST3. Raters involved in outcome testing were blind to the hypotheses and to participant group assignment. Therapists were not blind to the hypotheses. Participants could not be blinded to their group assignment, which is typical of nonpharmacological intervention trials, but they were not informed of the hypotheses or of which intervention was used as a control, to reduce expectancy effects. For each time point, outcome measures were taken during a single session. The order of presentation of the tasks was similar across participants and sessions and was planned to minimize interference effects between memory tasks. Alternative versions of the memory tasks were used for each time point and randomly allocated to participants. Participants were offered a make-up session whenever they missed a session. Participants who were present for at least 80% of the intervention and completed at least 80% of the homework were deemed to be adherent. The research conformed with the ethical rules for human experimentation stated in the Declaration of Helsinki and was approved by the Comité d’Éthique de la Recherche, Centre de Recherche de l’Institut Universitaire de Gériatrie de Montréal.

Participants

Participants were recruited from memory clinics. Psychometrists tested participants to characterize them before randomization using a standard clinical and neuropsychological assessment. Enrolled participants met the Petersen criteria for amnestic MCI (aMCI); for more details on baseline tests and inclusion and exclusion criteria, see, Table 1 and Supplementary Text S1.

Interventions

Both interventions were provided in small groups of 4 to 5 participants during 8 weekly 120-minute sessions and were constructed using a similar format. The single-session booster reviewed the procedures and strategies learned during the main intervention.

The MEMO program (¹⁸,¹⁹ for details) includes memory and attentional control strategies. Session 1 provides psychoeducational information regarding memory, health, and aging. Session 2 teaches participants to vary their attentional priority during dual tasking.²⁷⁻²⁹ because it was found that providing short attentional training improved the efficacy of subsequent memory training. In Session 3, participants learn to improve visual interactive imagery.
Figure 1. Flow diagram indicating participant progress through the trial.
abilities. \(^\text{30}\) In Session 4, participants learn the method of loci, during which they must generate a set of familiar locations and associate items with these locations. Session 5 teaches strategies to learn the names of new persons. In Session 6, participants learn the Preview, Question, Read, State, Test\(^\text{31}\) (PQRST) method to remember short text excerpts. In Sessions 7 and 8, the methods are reviewed, along with their applications in daily life, and techniques using verbal organization (e.g., semantic clustering) and external memory aids are presented. Generalization is fostered with homework exercises to practice the strategies in diverse situations, teaching multiple mnemonics to increase the likelihood that components of training will be appropriate for daily situations and by providing indications on the situations that optimize the use of particular strategies. Self-efficacy was promoted using modeling and grading of the level of task difficulty and by paying attention to individual differences in the ability to learn the strategies.

The content of the psychosocial intervention was based on the cognitive-behavioral approach, and aims to improve general psychological well-being. Session 1 focuses on psychoeducation, exploring the links between activities, aging, and psychological well-being. Participants are also invited to identify satisfactory aspects of their lives and to find ways to increase positive situations. Session 2 focuses on cognitive restructuring of thoughts, beliefs, and attitudes to help participants understand their relationships and modify thoughts that cause unhelpful emotions\(^\text{16}\) and

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### Table 1. Participant Clinical Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cognitive Training, n = 40</th>
<th>Psychosocial Intervention, n = 43</th>
<th>No-Contact Control, n = 44</th>
<th>(p)-Value*</th>
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<tbody>
<tr>
<td>Demographic</td>
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<tr>
<td>Age, mean ± SD</td>
<td>71.3 ± 8.5</td>
<td>72.1 ± 6.7</td>
<td>73.1 ± 6.5</td>
<td>0.51</td>
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<tr>
<td>Sex, n</td>
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<tr>
<td>Male</td>
<td>20</td>
<td>19</td>
<td>18</td>
<td>0.70</td>
</tr>
<tr>
<td>Female</td>
<td>20</td>
<td>24</td>
<td>26</td>
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<tr>
<td>Education, years, mean ± SD</td>
<td>14.5 ± 4.2</td>
<td>14.7 ± 3.5</td>
<td>14.8 ± 3.8</td>
<td>0.94</td>
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<tr>
<td>Memory assessment, mean ± SD</td>
<td></td>
<td></td>
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<tr>
<td>Montreal Cognitive Assessment (range 0–30)</td>
<td>24.1 ± 3.0</td>
<td>25.0 ± 2.7</td>
<td>24.2 ± 3.3</td>
<td>0.33</td>
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<tr>
<td>Free recall (range 0–16)</td>
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<tr>
<td>Immediate</td>
<td>14.1 ± 2.4</td>
<td>14.1 ± 2.5</td>
<td>14.1 ± 2.0</td>
<td>0.99</td>
</tr>
<tr>
<td>Delayed</td>
<td>7.8 ± 3.5</td>
<td>7.6 ± 3.8</td>
<td>7.3 ± 3.6</td>
<td>0.86</td>
</tr>
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<td>Rey Figure</td>
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<tr>
<td>Copy time, seconds</td>
<td>234 ± 102</td>
<td>246 ± 125</td>
<td>255 ± 147</td>
<td>0.75</td>
</tr>
<tr>
<td>Recall (3-minute delay) (range 0–36)</td>
<td>13.0 ± 6.6</td>
<td>11.3 ± 5.3</td>
<td>11.4 ± 6.8</td>
<td>0.40</td>
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<td>Stroop Victoria</td>
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<tr>
<td>Time on 3rd plate, seconds</td>
<td>37.1 ± 11.4</td>
<td>35.3 ± 12.6</td>
<td>37.3 ± 19.4</td>
<td>0.80</td>
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<td>Errors on 3rd plate (range 0–24)</td>
<td>1.5 ± 1.8</td>
<td>2.1 ± 2.1</td>
<td>1.9 ± 2.2</td>
<td>0.46</td>
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<tr>
<td>Neuropsychiatric assessment, mean ± SD</td>
<td></td>
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<td>Eysenck Personality Inventory (range 0–24)</td>
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<tr>
<td>Extraversion(^a)</td>
<td>10.6 ± 4.0</td>
<td>10.8 ± 3.7</td>
<td>10.3 ± 2.4</td>
<td>0.83</td>
</tr>
<tr>
<td>Neuroticism(^*)</td>
<td>8.1 ± 4.8</td>
<td>9.7 ± 4.3</td>
<td>8.7 ± 4.8</td>
<td>0.28</td>
</tr>
<tr>
<td>Routinization preference scale (range 0–24)(^d)</td>
<td>18.5 ± 5.7</td>
<td>18.3 ± 6.2</td>
<td>16.9 ± 5.2</td>
<td>0.37</td>
</tr>
<tr>
<td>Physical Activity Inventory (range 0–7)(^e)</td>
<td>2.5 ± 1.9</td>
<td>3.0 ± 1.8</td>
<td>2.6 ± 2.0</td>
<td>0.44</td>
</tr>
<tr>
<td>General Self-Efficacy Scale (range 10–40)(^f)</td>
<td>32.7 ± 4.9</td>
<td>30.9 ± 4.7</td>
<td>31.6 ± 5</td>
<td>0.24</td>
</tr>
<tr>
<td>Memory composite score, mean ± SD</td>
<td></td>
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</tr>
<tr>
<td>Immediate</td>
<td>0.02 ± 0.89</td>
<td>0.02 ± 0.99</td>
<td>-0.05 ± 0.77</td>
<td>0.91</td>
</tr>
<tr>
<td>Delayed</td>
<td>-0.01 ± 0.89</td>
<td>0.04 ± 0.95</td>
<td>-0.04 ± 0.78</td>
<td>0.91</td>
</tr>
<tr>
<td>Psychological health measures, mean ± SD</td>
<td></td>
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<tr>
<td>Geriatric Depression Scale score (range 0–15)</td>
<td>3.0 ± 3.1</td>
<td>3.6 ± 3.2</td>
<td>3.2 ± 2.8</td>
<td>0.70</td>
</tr>
<tr>
<td>Geriatric Anxiety Scale score (range 0–20)</td>
<td>4.9 ± 5.0</td>
<td>5.4 ± 4.7</td>
<td>5.4 ± 5.1</td>
<td>0.88</td>
</tr>
<tr>
<td>Well-being (range 0–105)</td>
<td>74.0 ± 16.0</td>
<td>72.0 ± 15.0</td>
<td>72.0 ± 15.0</td>
<td>0.88</td>
</tr>
<tr>
<td>Distal outcome measures, mean ± SD</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Strategy use in daily life (Metamemory Questionnaire) (range 0–96)</td>
<td>44.0 ± 16.0</td>
<td>44.0 ± 12.0</td>
<td>40.0 ± 14.0</td>
<td>0.29</td>
</tr>
<tr>
<td>Complex activities of daily living (Activities of Daily Living–Prevention Instrument) (range 0–45)</td>
<td>39.0 ± 4.9</td>
<td>40.0 ± 5.5</td>
<td>38.0 ± 5.1</td>
<td>0.23</td>
</tr>
<tr>
<td>Self reported memory (Questionnaire d’Auto-Evaluation de la Mémoire) (range 1–6)</td>
<td>2.7 ± 0.7</td>
<td>2.7 ± 0.6</td>
<td>2.6 ± 0.6</td>
<td>0.82</td>
</tr>
</tbody>
</table>

\(^a\) \(p\)-value for analysis of variance group effect. None of the measures had a significant group effect.

\(^*\) Higher scores indicate more extraversion.

\(^\dagger\) Higher scores indicate more neuroticism.

\(^\text{d}\) Higher scores indicate more routinization.

\(^\text{e}\) Higher scores indicate more physically active.

\(^\text{f}\) Higher scores indicate higher self-efficacy.

SD = standard deviation.
includes diaphragmatic breathing. Sessions 3 and 4 consist of behavioral activation to increase the level of daily activities. Session 5 introduces participants to problem-solving skills, for instance, ways to manage stressful life events. In Session 6, participants learn to manage their anger and frustration. Sessions 7 and 8 review key concepts and consolidate knowledge.

Therapists were qualified clinicians and received 16 hours of training. Different therapists were used for the psychosocial and cognitive interventions to avoid contamination.

Proximal Outcome Measures

Cognitive Measures

Immediate and delayed episodic memory composite scores determined from pooling Z-scores of the word list and face-name association tasks were used as proximal outcome measures for the cognitive training program. A previous study reported that the 2 tasks were sensitive to cognitive intervention.\(^4\) Composite scores were used to reduce the number of comparisons and the effect related to the specific characteristics of the tests.

Psychological Health Measures

Three reliable, valid measures of psychological health were used as proximal outcome measures for the psychosocial intervention: the Geriatric Anxiety Inventory,\(^3\) the General Self-Efficacy Scale,\(^3, 4\) and the General Well-Being Schedule.\(^5, 6\)

Distal Outcome Measures

Distal outcomes were reliable, valid measures of generalization to everyday life. The Multifactorial Memory Questionnaire—Memory Strategies measures how frequently participants use memory strategies in everyday life. The Questionnaire d’Auto-Évaluation de la Mémoire measures subjective complaints. The Activities of Daily Living—Prevention Instrument questionnaire (ADL-PF) measures difficulties in performing complex activities of daily living.

Moderators

To assess moderators of treatment effect, we used age; education; sex; baseline delayed free recall condition score from the Free and Cued Recall memory test used in the clinical battery; the neuroticism, introversion, and extraversion scales of the Eysenck Personality Inventory; the Echelle de Préférence de Routinisation, which measures whether individuals engage in routinized behaviors; the Inventaire d’Activités Physiques, a physical activity inventory; and the General Self-Efficacy Scale.

Statistical Methods

The primary efficacy analysis was based on a modified intention-to-treat analysis (mITTA), including data from participants who completed at least one postbaseline assessment to minimize attrition-related bias at follow-up while maintaining treatment integrity. Group differences on baseline characteristics of the mITTA sample were assessed using separate analyses of variance. Efficacy and durability analyses were conducted using mixed linear models. The fixed effects were intervention (cognitive, psychosocial, no contact), time (PRE, POST, POST3, POST6), and their interaction. A significant interaction is expected if the intervention is more beneficial than the no-contact condition. When an interaction was found, we examined whether there was a significant difference between PRE and POST in each group and assessed change scores at posttraining ([PRE−POST]/PRE), [PRE−POST3]/PRE, [PRE−POST6]/PRE). Efficacy is supported if the POST change score is larger in the intervention than the no-contact group. Durability is supported if the POST3 or POST6 change score is larger in the intervention than in the no-contact group. All analyses were adjusted for sex, age, and education, and normalized scores were used for psychological and generalization measures to facilitate comparison across variables. Finally, we used stepwise regression analyses with the per-protocol participants from the cognitive training group to explore whether the moderators predicted delayed memory change scores at the 3 time points. Detailed results and statistical analyses are provided in Supplementary Tables S1–S3).

RESULTS

The sample size was determined from pilot data that indicated medium to moderate effect sizes.\(^2\) Of the 162 participants initially planned, 153 were eligible, 145 agreed to be randomized (Figure 1), 127 completed at least 1 post-training assessment (87.6%) and were included in the mITTA, 114 completed POST3 (78.6%), and 104 completed POST6 (71.7%). The numbers of retained participants were equivalent across intervention conditions (POST: Pearson chi-square (4) = 2.192, \(P = .33\); POST3: Pearson chi-square (4) = 0.804, \(P = .67\); POST6: Pearson chi-square (4) = 5.941, \(P = .20\)).

The mean age of the mITTA sample was 72.2 ± 7.2, mean education was 14.7 ± 3.8 years, and average Montreal Cognitive Assessment score was 24.4 ± 3; 55% of the mITTA sample were women. Table 1 reports baseline characteristics of the mITTA sample as a function of intervention condition. There were no group differences at baseline in demographic or clinical characteristics.

Cognitive Outcomes

Figure 2A shows results for the cognitive outcomes. An intervention-by-time interaction is expected to support a training effect. The mixed model indicated a main effect of time (\(F = 8.404, P < .001\)), age (\(F = 13.868, P < .001\)), and education (\(F = 6.119, P = .01\)) and an intervention-by-time interaction (\(F = 3.381, P = .003\)). The estimated delayed memory mean change score for the cognitive training group (using the PRE and control groups as reference points) was 0.35 at POST (95% confidence interval (CI) = 0.06–0.64), 0.33 at POST3 (95% CI = 0.03–0.64), and 0.52 at POST6 (95% CI = 0.22–0.82). Estimated delayed memory mean change scores for the psychosocial
intervention group were −0.11 at POST (95% CI = −0.40–0.18), 0.09 at POST3 (95% CI = −0.20–0.39), and −0.07 at POST6 (95% CI = −0.37–0.23). Delayed memory scores increased from PRE to POST (P = .02), POST3 (P = .03), and POST6 (P = .001) for the cognitive training group only. The mixed model for the immediate memory score indicated a main effect of time (F = 4.594, P = .004), age (F = 14.905, P < .001), and education (F = 5.992, P = .01) but no intervention-by-time interaction (F = 0.796, P = .57). Estimated mean change scores for the immediate memory score were 0.09 (95% CI = −0.09–0.28) at POST, 0.07 at (95% CI = −0.13–0.27) POST3, and 0.07 (95% CI = −0.012–0.27) at POST6.

Psychosocial Outcomes

Figure 2B presents the psychosocial measures. The mixed model on anxiety symptoms (Geriatric Anxiety Inventory) revealed no Intervention × Time interaction (F = 0.454, P = 0.84), but only a Sex (F = 7.806, P = .006 due to lower score in men), and Education effect (F = 9.941, P = .002. None of the effects were significant for depressive symptoms (Geriatric Depression Scale), including the intervention-by-time interaction (F = 0.572, P = .75). The analysis of well-being revealed an effect of sex (F = 7.543, P = .007; due to higher score in men) but no intervention-by-time interaction (F = 0.366, P = .90).
Generalization Outcomes

Generalization measures are presented in Figure 2C. There was an intervention-by-time interaction for strategy use (Metamemory Questionnaire) \( (F = 3.804, P = .001) \). Estimated mean change scores for strategy use were 0.33 (95% CI = 0.02–0.63) at POST, 0.31 (95% CI = 0.00–0.63) at POST3, and 0.38 (95% CI = 0.07–0.69) at POST6 in the cognitive training group and −0.35 (95% CI = −0.65 to −0.06) at POST, −0.03 (95% CI = −0.35–0.27) at POST3, and −0.04 (95% CI = −0.35–0.27) at POST6 in the psychosocial intervention group. The cognitive training group showed a significant increase in strategy use from PRE to POST \( (P = 0.03) \) and POST6 \( (P = 0.01) \). The effect just missed significance at POST3 \( (P = .05) \). In contrast, there was a significant decrease at POST3 \( (P = 0.02) \) for the psychosocial training group. There was an effect of sex \( (F = 15.268, P < .001) \) on the ADL-PI because of lower scores in men but no intervention-by-time interaction \( (F = 1.624, P = .14) \). The analysis of memory complaint (Questionnaire d’Auto-Évaluation de la Mémoire) revealed a global effect of time \( (F = 3.512, P = .02) \) because participants reduce their level of complaints from PRE to POST but no intervention-by-time interaction \( (F = 0.650, P = .69) \).

Moderators

A larger delayed memory change score at POST was associated with a larger routinization score (Échelle de Préférence de Routinisation), accounting for 9% of the variance. At POST3, a larger delayed memory change score was associated with greater self-efficacy and routinization and better free recall, accounting for 32% of the variance. Greater routinization and self-efficacy were associated with a larger delayed memory change score at POST6, accounting for 26% of the variance.

DISCUSSION

We report the first randomized controlled study comparing the efficacy of cognitive training in aMCI with that of a waitlist and an active control condition involving a psychosocial intervention. We found a significant efficacy effect for the delayed memory score, and the effect was durable, lasting at least 6 months after training. These positive results are consistent with those reported by a few prior studies that used smaller samples and less stringent designs.9,10,18 This study has many strengths over those previously published. One was that transfer to activities of daily living was measured, because a question that is frequently asked is whether people use the strategies learned in their daily lives. Cognitive training increased self-reported use of strategies in daily life, suggesting that the intervention broadened the range of strategies that persons with MCI can use to improve their day-to-day life, although we did not find that cognitive training improved activities of daily living or decreased the general level of memory complaint. This might be because of the low level of functional impairment in MCI, a lack of sensitivity of self-reported measures, or the relatively short follow-up. This may also reflect a null effect, which would be consistent with many studies failing to observe transfer to non-cognitive outcome domains.10 Training type may also be a factor; process-based techniques might transfer more broadly than strategy-based training.47

Our inclusion of personality measures to characterize responders is an additional strength of the study. It showed that people who respond well are those with more self-confidence and who enjoy structure in their lives. Education, sex, and age did not emerge as reliable predictors of efficacy, suggesting that personality characteristics determine individual response to cognitive training more than demographic characteristics.

Given the debate regarding the use of active control groups, even though the psychosocial intervention was meant to be a very active control group, it had no effect on cognition. Furthermore, neither the cognitive training nor the psychosocial intervention improved the mood or well-being of participants, which was surprising considering that psychological symptoms are often present in MCI. Individuals with active psychiatric problems were excluded, so participants had low depressive and anxiety scores overall. Future work will be required to assess whether different interventions might be more appropriate to improve psychological health or whether this type of intervention might be more appropriate in individuals with particular types of MCI, for instance those with more depressive symptomatology or those with lower level of well-being.

This study has some limitations. The training was short, and a larger dose might have increased the magnitude of the effect, particularly for the psychosocial intervention. Also, the study was not designed to assess the effect on progression to dementia, and we did not use biomarkers.

Overall, our positive results justify the inclusion of cognitive training as an approach to help cognitively vulnerable older adults and possibly to prevent dementia in at-risk individuals.48, 49 Future research should include assessment of the combined value of cognitive and psychosocial treatments, use of this intervention in combination with pharmacotherapy or with stimulating leisure activities, and assessment of neural substrates of clinical improvement using brain imagery techniques.

ACKNOWLEDGMENTS

The authors wish to acknowledge the contribution of Emmanuelle Lepage and Isabelle Tremblay in coordinating the trial and of Samira Mellah for her support in the statistical analyses and in preparing the tables and figures. Gabrielle Ciquier, a medical editor, reviewed the article for grammar and clarity of writing.

Financial Disclosure: Funded by the Canadian Institutes for Health Research.

Conflict of Interest: Sylvie Belleville receives research grants from the Fonds d’Innovation Pfizer-FRQS for Alzheimer disease and related diseases for the Consortium pour l’identification précoce de la Maladie d’Alzheimer—Québec (CIMA-Q). She has been a consultant for research development on the prevention of Alzheimer’s disease for the Fondation IUGM (2016) and a consultant for the development
of a cognitive stimulation program for the Centre de promotion de la Santé AvantAge (2015). She has intellectual property rights on the Programme de Stimulation pour une santé cognitive, Memoria, Batterie d’évaluation de la mémoire Côte-des-Neiges and MEMO, Programme pour une mémoire optimale. Carol Hudon received a research grant from the Fonds d’Innovation Pfizer-FRQS for Alzheimer’s disease and related diseases for the CIMA-Q. He has been a rater in clinical trials (Lundbeck, Roche) and a consultant for Bracket Global. Sebastien Grenier has intellectual property rights on the Programme d’intervention psychosociale axé sur le bien être psychologique. Brigitte Gilbert was a consultant for the development the Ateliers de stimulation pour une santé cognitive (2014). She has intellectual property rights on MEMO: Méthode d’entraînement pour une mémoire optimale, 2007. Marie-Christine Ouellet has intellectual property rights on the Programme d’intervention psychosociale axé sur le bien être psychologique. Chantal Viscogliosi is responsible for the training and for a forum on assessment and intervention for older adults with cognitive impairment at the Ordre des Ergothérapeutes du Québec. She conducts training for multidisciplinary teams in cognitive strategies with older adults with cognitive disorders. She has intellectual property on the Programme Gymnastique des cellules grises. Serge Gauthier reports grants and personal fees from Lilly, TauRx, and Lundbeck; grants from Roche; and personal fees from Eisai and Schwabe.

**Author Contributions:** Belleville: Study concept and design, construction of cognitive intervention, organization of data acquisition at Montreal site, data analyses, writing first version of manuscript. Hudon: Study concept and design, organization of data acquisition at Quebec site, revision of manuscript. Bier, Brodeur, Viscogliosi, Gauthier: Study concept and design, revision of manuscript. Gilbert: Study concept and design, construction of cognitive intervention, participation in psychosocial training, revision of manuscript. Ouellet, Grenier: Study concept and design, construction of content of psychosocial training, revision of manuscript.

**Sponsor’s Role:** This work was supported by a grant from the Canadian Institutes for Health Research (MOP115086). CH, MCO, SGre, and NB were supported by Bracket Global. Sebastien Grenier has intellectual property rights on the Programme de Stimulation pour une santé cognitive (2014). She has intellectual property on the Programme Gymnastique des cellules grises. Serge Gauthier reports grants and personal fees from Lilly, TauRx, and Lundbeck; grants from Roche; and personal fees from Eisai and Schwabe.

**REFERENCES**


SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Text S1 Criteria for amnestic mild cognitive impairment, exclusion criteria and Tests used for clinical characterization.

Table S1 Mean scores (SD in parentheses) on the outcome variables at PRE, POST, POST3 and POST6

Table S2 Output of the mixed linear model for the immediate memory composite score and delayed memory composite score

Table S3 Regression models and factors that predict the cognitive training effect on the delayed memory composite score at POST, POST3 and POST6

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