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RESEARCH ARTICLE

Five-year effects of cognitive training in individuals with mild cognitive impairment

Sylvie Belleville[1,2] | Marc Cuesta[1] | Nathalie Bier[1,2] | Catherine Brodeur[1,2] | Serge Gauthier[3] | Brigitte Gilbert[1] | Sébastien Grenier[1,2] | Marie-Christine Ouellet[4] | Chantal Viscogliosi[5] | Carol Hudon[4,6]

[1]Research Centre, Institut universitaire de gériatrie de Montréal, Montreal, Canada

[2]Université de Montréal, Montreal, Canada

[3]Research Center for Studies in Aging, McGill University, Canada Research Center on Aging, Montreal, Canada

[4]École de psychologie, Université Laval, Quebec, Canada

[5]Centre intégré universitaire de santé et de services sociaux (CIUSSS) de l'Estrie - Centre hospitalier universitaire de Sherbrooke, Université de Sherbrooke, Sherbrooke, Canada

[6]CERVO Research Centre and Université Laval, Quebec, Canada

Correspondence
Sylvie Belleville, Research Centre, Institut universitaire de gériatrie de Montréal, Montreal, Canada, H3W 1W5.
Email: sylvie.belleville@umontreal.ca

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Abstract

INTRODUCTION: In a 5-year follow-up study, we investigated the enduring effects of cognitive training on older adults with mild cognitive impairment (MCI).

METHODS: A randomized controlled single-blind trial involved 145 older adults with MCI, assigned to cognitive training (MEMO+), an active control psychosocial intervention, or a no-contact condition. Five-year effects were measured on immediate and delayed memory recall, the Montreal Cognitive Assessment screening test (MoCA), self-reported strategy use, and daily living difficulties.

RESULTS: At follow-up, participants who received cognitive training showed a smaller decline in delayed memory and maintained MoCA scores, contrasting with greater declines in the control groups. Cognitive training participants outperformed controls in both delayed memory and MoCA scores at the 5-year time point. No significant group differences were observed in self-reported strategy use or difficulties in daily living.

DISCUSSION: Cognitive training provides long-term benefits by mitigating memory decline and slowing clinical symptom progression in older adults with MCI.

KEYWORDS
cognition, cognitive training, long-term benefit, mild cognitive impairment, psychosocial intervention

Highlights

- Cognitive training reduced the 5-year memory decline of persons with MCI.
- Cognitive training also reduced decline on the Montreal Cognitive Assessment (MoCA).
- No intervention effect was found on strategy use or activities of daily living.

1 | INTRODUCTION

Alzheimer's disease (AD) has a long prodromal phase, offering a valuable opportunity to implement strategies aimed at slowing the progression of mild cognitive symptoms into dementia.[1–3] Among these strategies, cognitive training emerges as a promising approach to counter cognitive decline in individuals with mild cognitive impairment (MCI),[4–7] many of whom find themselves in the prodromal phase of AD. Cognitive training equips older adults with compensatory strategies that mitigate the impact of cognitive difficulties in their daily lives. Furthermore, it contributes to cognitive reserve, providing additional protection against dementia.[8–10]

Studies have indicated that cognitive training can yield immediate cognitive benefits in individuals with MCI.[5,11–13] However, long-term effects of cognitive training in this population and its efficacy in mitigating the progression of cognitive symptoms remain largely unknown. In the context of normal aging, the ACTIVE trial[14] stands out as one of the few studies that examined the long-term benefits of cognitive training, including follow-up assessments up to 10 years post-intervention.[15,16] Participants randomized to memory, reasoning, or processing speed training outperformed a no-contact control group in the targeted cognitive domains. Notably, those in the reasoning and processing speed groups maintained superior performance 5[15] and 10 years[16] post-training. Nevertheless, the ACTIVE trial exclusively involved healthy older adults, and to our knowledge, no study has assessed the long-term benefits of cognitive training on cognition in individuals with MCI beyond an 18-month follow-up.[13] Demonstrating that cognitive training can reduce symptom progression holds significant potential, particularly in the absence of disease-modifying treatments. It could serve as an accessible tool to support cognition in older adults at risk of dementia.

Over the past 15 years, we have developed and validated the MEMO+ program (*Méthode d'Entrainement pour une Mémoire Optimale*, Training Method for Optimal Memory[5,17,18]). This program teaches memory encoding strategies that utilize the remaining cognitive capacities of individuals with MCI, helping them in compensating for their everyday memory challenges. A prior randomized controlled trial involving 145 older adults with MCI demonstrated the program's short-term efficacy in improving episodic memory, showing enhanced delayed memory compared to a no-contact control group.[5], while a psychosocial intervention (active control) did not. Participants also reported using more memory strategies in daily life, as measured by the Multifactorial Memory Questionnaire-Strategies (MMQ).[19] Enhanced delayed memory and strategy use effects were still observed 6-months post-intervention. Furthermore, increased activation in frontal, temporal, and parietal brain regions was observed,[18] suggesting enhanced recruitment of both specialized and alternative brain regions.

The main objective of the present study was to assess the long-term benefits of the MEMO+ cognitive training program. To accomplish this objective, we contacted participants from the initial MEMO+ study 5 years after training. We conducted assessments focusing on delayed memory, which was identified as the primary outcome sensitive to MEMO+ training in the initial study. Additionally, we investigated potential maintenance of self-reported difficulties in activities of daily living (ADL), of global cognition with the Montreal Cognitive Assessment (MoCA)[20] and of strategy use with the MMQ questionnaire. Given that the participants had MCI at study entry, we hypothesized that there would be a decline in delayed memory and MoCA scores at the 5-year follow-up, along with an increase in self-reported difficulties in ADL. However, we anticipated a significant Intervention × Time interaction, indicating that participants randomized to the MEMO+ program would exhibit less memory decline and fewer self-reported difficulties in ADL than those in the no-contact condition. Furthermore, we expected MEMO+ participants to continue reporting greater use of memory strategies on the MMQ than participants in the no-contact condition. Finally, based on the hypothesis that cognitive training has a protective effect, we anticipated that MEMO+ participants would better maintain their performance on the MoCA compared to participants in the no-contact condition.

RESEARCH IN CONTEXT

1. **Systematic review**: There is a paucity of published data on the long-term effect of non-pharmacological interventions, such as cognitive training.
2. **Interpretation**: Following a 5-year follow-up, individuals with mild cognitive impairment who underwent cognitive training exhibited significantly less memory decline and outperformed the control groups on the Montreal Cognitive Assessment (MoCA). No intervention effects were observed on self-reported strategy use or difficulties in instrumental activities of daily living at the 5-year timepoint.
3. **Future directions**: Cognitive training shows promise for providing long-term benefits to older adults with mild cognitive impairment; however, larger studies are needed, and efforts should focus on identifying those who benefit and on developing approaches that facilitate effective transfer.

2 | METHODS

2.1 | Design and participants

The MEMO+ is a multicenter, randomized controlled clinical trial (for details, see Refs.[5,21]). Participants were recruited from memory clinics between April 2012 and April 2015 across two Canadian sites (Montreal and Quebec City). At the study onset, participants were older adults meeting the clinical criteria for amnestic single or multiple domain MCI (i.e., a self-reported memory complaint and an objective memory deficit, defined as performance at least 1.5 standard deviations (SD) below the average level of same-age peers without

TABLE 1 Participants' demographic and clinical characteristics for the mITT and POST5y sample.

	Cognitive training		Psychosocial intervention		No-contact		
	mITT (*N* = 40)	POST5y (*N* = 17)	mITT (*N* = 43)	POST5y (*N* = 21)	mITT (*N* = 44)	POST5y (*N* = 21)	*p* value for group effect at POST5y
Age PRE: mean year (SD)	71.3 (8.5)	71.2 (8.2)	72.1 (6.7)	72.1 (7.4)	73.1 (6.5)	70.9 (6.5)	0.85
Sex: male, female	20, 20	6, 11	19, 24	10, 11	18, 26	11, 10	0.56
Education: mean year (SD)	14.5 (4.2)	14.7 (3.8)	14.7 (3.5)	15.1 (4.0)	14.8 (3.8)	16.6 (3.5)	0.25
MoCA PRE: mean score (SD)	24.1 (3.0)	24.8 (2.5)	25.0 (2.7)	25.1 (3.2)	24.2 (3.3)	26.0 (2.3)	0.35
Genotype APOE4[a]: number with at least one allele (%)	8/17 (47.0%)		5/21 (23.8%)		6/21 (28.6%)		0.25

Note: mITT: modified-intention-to-treat: participants who participated in at least one of the post-intervention assessments. POST5y: participants who returned for the 5-year assessment.
Abbreviations: MoCA, Montreal cognitive assessment; PRE, pre-intervention; SD, standard deviation.
[a]Genotype data available for a subset of participants tested at POST5y.

adjustment for education) with or without additional deficits on non-memory tests but without evidence of dementia.[22] Before randomization, a standard clinical and neuropsychological assessment was performed to characterize the participants and determine their eligibility based on inclusion and exclusion criteria (Table 1 and Refs.[5,21]).

Participants were randomly assigned to one of three intervention groups: cognitive training, psychosocial intervention (active control), or no-contact condition. Over a 2-month period, participants underwent eight 120-min weekly training sessions. Assessments were conducted at several time points: pre-intervention (PRE), 1-week post-intervention (POST), 3-months post-intervention (POST3m), 6 months post-intervention (POST6m), and 5 years post-intervention (POST5y). The initial study was registered (NCT01448148). The current study was conducted in accordance with the Declaration of Helsinki and approved by the Research Ethics Board (REB) vieillissement-neuroimagerie of the CIUSSS-CSMTL (#11-12-017), and the Quebec City REB (approval #282-2011).

2.2 | Interventions

Both the cognitive and psychosocial interventions comprised eight 2-h small-group sessions (refer to the appended material for rationale and detailed description). The cognitive intervention focused on teaching a set of memory strategies (i.e., visual imagery, method of loci, face-name association, semantic organization) and attention control strategies using the MEMO+ program.[5,21] This intervention was designed to develop self-efficacy and metacognition, both recognized as influential factors in older adults' ability to acquire and apply new knowledge. It also provided guidance on integrating these learned strategies into daily life, incorporating at-home exercises to facilitate their application to real-world situations. The psychosocial intervention aimed to improve overall psychological well-being through a program based on the cognitive-behavioral approach. It encompassed techniques such as behavioral activation, cognitive restructuring, anger and stress management, and problem-solving tailored to daily-life.

Both interventions included homework, and participants attended a booster session approximately 1 week after the POST3m assessment to review previously learned procedures and strategies. For ethical reasons, an abbreviated four-hour version of the MEMO+ program (short MEMO or sMEMO) was offered as an option to participants in both the active control and no-contact conditions within a year following the study's conclusion. Further details regarding the analyses and results concerning the effect of sMEMO are available in the Supplementary Material S1.

2.3 | Outcome measures

For the POST5y assessment, we included a subset of the initial outcome measures to reduce participant burden while optimizing participation rates. This assessment had a duration of 30–40 min. Memory was measured using a 12-word list recall task, where words were visually and simultaneously presented for a 2-min study period. Immediate and delayed recalls were performed after a 30-s and a 10-min delay, respectively, during which non-interfering tasks were performed. However, the analysis focused on delayed recall, as it exhibited an effect in the original study[5] and delayed recall is also a more sensitive measure of MCI progression to dementia compared to immediate recall.[23] Self-assessment of instrumental ADL was conducted using the Activities of Daily Living—Prevention Instrument questionnaire (ADL-PI),[24] which included questions about difficulties encountered while performing complex activities such as driving, cleaning, and cooking. The integration of strategies into daily life was evaluated through the MMQ, where participants rated their use of memory strategies in real-world situations. General cognitive performance and clinical status were measured using the MoCA, a concise screening tool designed to assess various cognitive domains, including memory, attention, language, reasoning, and visuo-spatial abilities.

2.4 | Consent statement

All human subjects provided informed consent for their participation in this study.

2.5 | Statistical analysis

All statistical tests were two-tailed with statistical significance determined as a p value < 0.05. Effect sizes were provided when relevant.

Group differences (cognitive training, psychosocial intervention, no-contact) in terms of age, education, and MoCA score at baseline were assessed using per-protocol data with one-way ANOVA. Group differences for sex were analyzed using a χ^2 test. We also examined the socio-demographic characteristics of participants tested in the POST5y assessment and compared them with those who were not assessed (shown in appended material).

To assess the intervention effects, a modified intention-to-treat (mITT) analysis was conducted using linear mixed-models (LMM) in all individuals tested at baseline who participated in at least one of the post-intervention assessments (POSTx; $n = 127$). The model included Time (PRE, POST, POST3m, POST6m, POST5y), Group (cognitive training, psychosocial intervention, no-contact) as fixed factors, as well as Time X Group interaction, and participant as a random effect. The LMM only included a random intercept as the addition of a random slope (after testing various covariance structures) did not improve the model. Control variables included years of education, sex, baseline, age, and MoCA score, without interaction terms. As the MoCA was not assessed at POST6m (to reduce repetition effects), the Time effect was modeled for PRE, POST, POST3m, and POST5y for this variable.

Time effects at any post-intervention time point for the cognitive training and psychosocial intervention groups were extracted from the LMM and calculated by comparing mean improvement from PRE to POSTx, with that of the no-contact group. We also computed Cohen's d effect sizes and their 95% confidence interval (CI)[25] to quantify the mean difference between one of the intervention groups and the no-contact group.[16]

To determine the proportion of participants exhibiting reliable change at POST5y in each group for each outcome, we used the standard error of measurement (SEM),[26,27] a statistical tool previously utilized in training studies.[14,16] Thresholds for reliable improvement and deterioration were set at 0.66 SEM and −0.66SEM, respectively.[16] In essence, an individual's POST5y score for a given outcome was considered improved compared to the PRE score if their difference equaled or exceeded the 0.66 SEM value. Conversely, if this difference was equal to or lower than the −0.66 SEM value, the POST5y score was deemed deteriorated relative to the PRE score. Subsequently, using a z-test, we assessed whether the proportion of participants showing reliable improvement or reliable deterioration differed in the cognitive training group compared to the psychosocial intervention group and no-contact group.

Given our interest in calculating the net effect of the training 5 years after its completion, and acknowledging results published from prior assessments, we primarily focused on the POST5y training effect unless otherwise specified.

3 | RESULTS

3.1 | POST5y sample characteristics

Out of the initial 127 mITT participants, we successfully contacted 89 individuals (38 were unreachable). Among those contacted, 59 agreed to participate in the POST5y assessment (59/127: 46.5%) (see Figure 1 for participant flow-chart and reasons for drop-out). Notably, most participants who did not return for the 5-year assessment were unreachable. Table 1 provides an overview of the characteristics of both the initial mITT sample and the POST5y sample. On average, participants completed the POST5y assessment 57 ± 9 months after finishing their initial training. Of the 59 POST5y participants, 17 were from the cognitive training group, 21 from the psychosocial intervention, and 21 from the no-contact group. Baseline characteristics were similar across all groups, as shown in Table 1. When comparing the baseline characteristics of participants who returned for the POST5y assessment to those who did not (see appended material), we found them to be largely comparable, with the exception of education, which was slightly higher among those who returned. It is worth noting that education is one of the variables controlled for in statistical analyses. Seventeen participants from the psychosocial intervention and 16 from the no-contact group had completed the sMEMO training (Figure 1).

3.2 | Memory

Figure 2A shows performance on the delayed memory score at the 5 time points. The LMM analysis for the delayed memory score revealed no significant effect of Group, $F(2,123.9) = 2.5$, $p = 0.08$, but indicated a significant effect of Time, $F(4,400.4) = 17.4$, $p < 0.001$, as well as a Group × Time interaction $F(8,400.5) = 3.4$, $p < 0.001$. Compared to the no-contact group, the cognitive training group exhibited a significant improvement in the delayed memory score from PRE to POST3m (mean change = 0.9, $p = 0.04$, d = 0.37, 95% CI [0.01, 0.73], POST6m (mean change = 1.6, $p < 0.001$, d = 0.65, 95% CI [0.30, 1.01]), and POST5y (mean change = 1.6, $p = 0.004$, d = 0.68, 95% CI [0.22, 1.15], with a medium effect size observed at POST 5y (Table 2). No change was observed for the psychosocial intervention at any time point. For reference, a significant decrease in the delayed memory score from PRE to POST5y was observed in the no-contact group ($p < 0.001$; d = −0.69, 95% CI [−1.01, −0.38]).

At POST5y, a reliable improvement in the delayed memory score was observed in 52.9% of participants from the cognitive training group, a proportion significantly higher than that found in both the psychosocial group (19.0%, $z = 2.2$, $p = 0.029$) and no-contact group

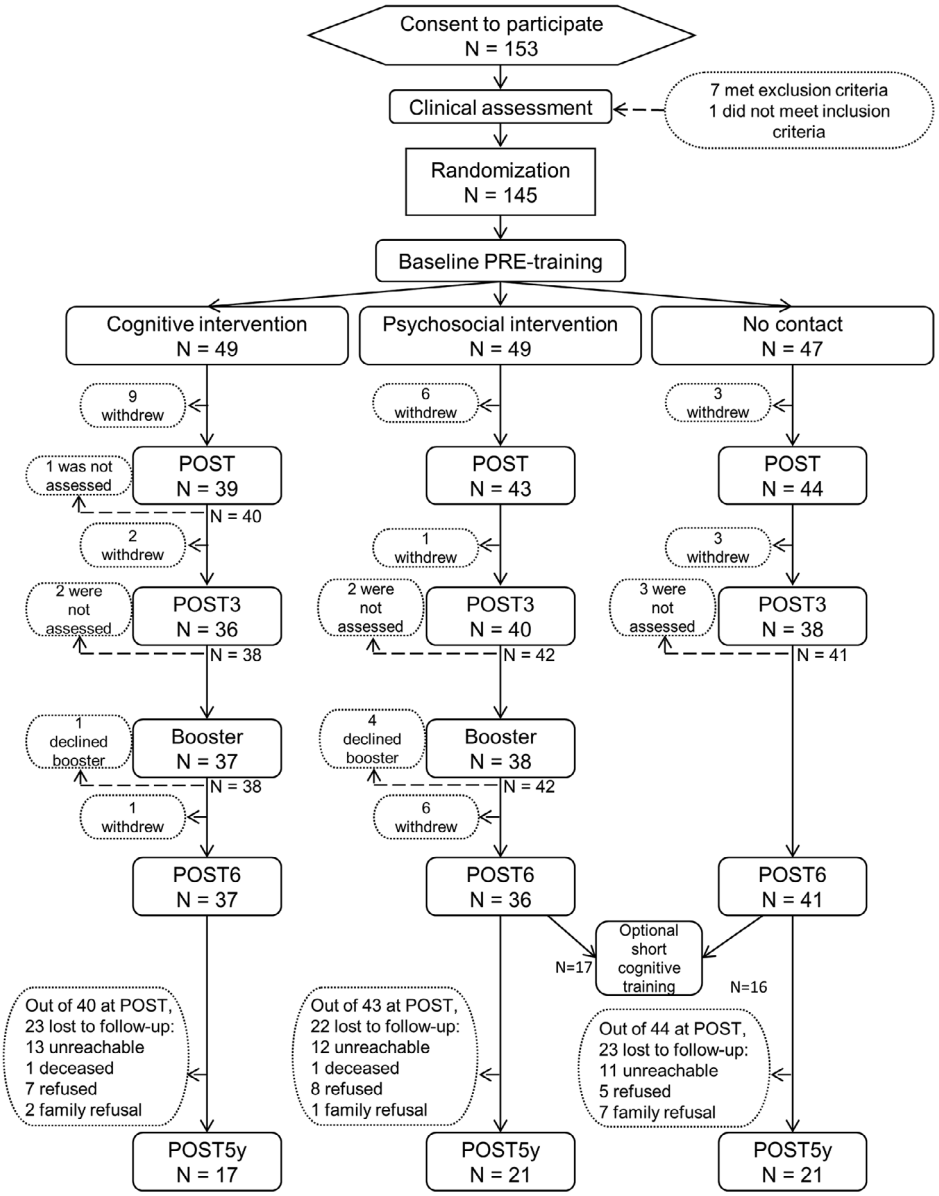

FIGURE 1 Flow diagram. The flow diagram shows the participant's progress throughout the trial. POST, post-intervention; POST3, 3 months post-intervention, POST6, 6 months post-intervention, POST5y, 5 years post-intervention; PRE, pre-intervention.

(19.0%, $z = 2.2$, $p = 0.029$) (Table 2). A reliable deterioration was observed in 23.5% of participants from the cognitive training group, which was comparable to the psychosocial group (28.6%, z = 0.4, $p = 0.73$), but lower than the no-contact group (47.6%, $z = 1.5$, $p = 0.12$).

3.3 | Instrumental ADL

Figure 2B shows the ADL-PI scores. The LMM indicated a significant effect of Time, $F(4,394.4) = 5.2$, $p < 0.001$, but no significant effect of Group, $F(2,123.9) = 0.8$, $p = 0.44$, or Time × Group interaction, $F(8,394.5) = 1.1$, $p = 0.34$. ADL-PI scores were generally lower at POST5y compared to baseline, irrespective of the intervention type (Figure 2B, Table 2).

Approximately 18.8% of cognitive training group participants exhibited reliable ADL-PI score improvement, a proportion which did not statistically differ from the psychosocial intervention group (9.5%, $z = 0.8$, $p = 0.41$) and no-contact group (28.6%, $z = 0.7$, $p = 0.49$) (Table 2). Within the cognitive intervention group, 62.5% displayed reliable deterioration at POST5y, a proportion similar to the psychosocial intervention group (42.9%, $z = 1.2$, $p = 0.24$) and the no-contact control group (42.9%, $z = 1.2$, $p = 0.24$).

3.4 | Memory strategy use

Scores on the memory strategy use are presented in Figure 2C. The LMM showed no effect of Time, $F(2,393.2) = 1.7$, $p = 0.1$, but did reveal

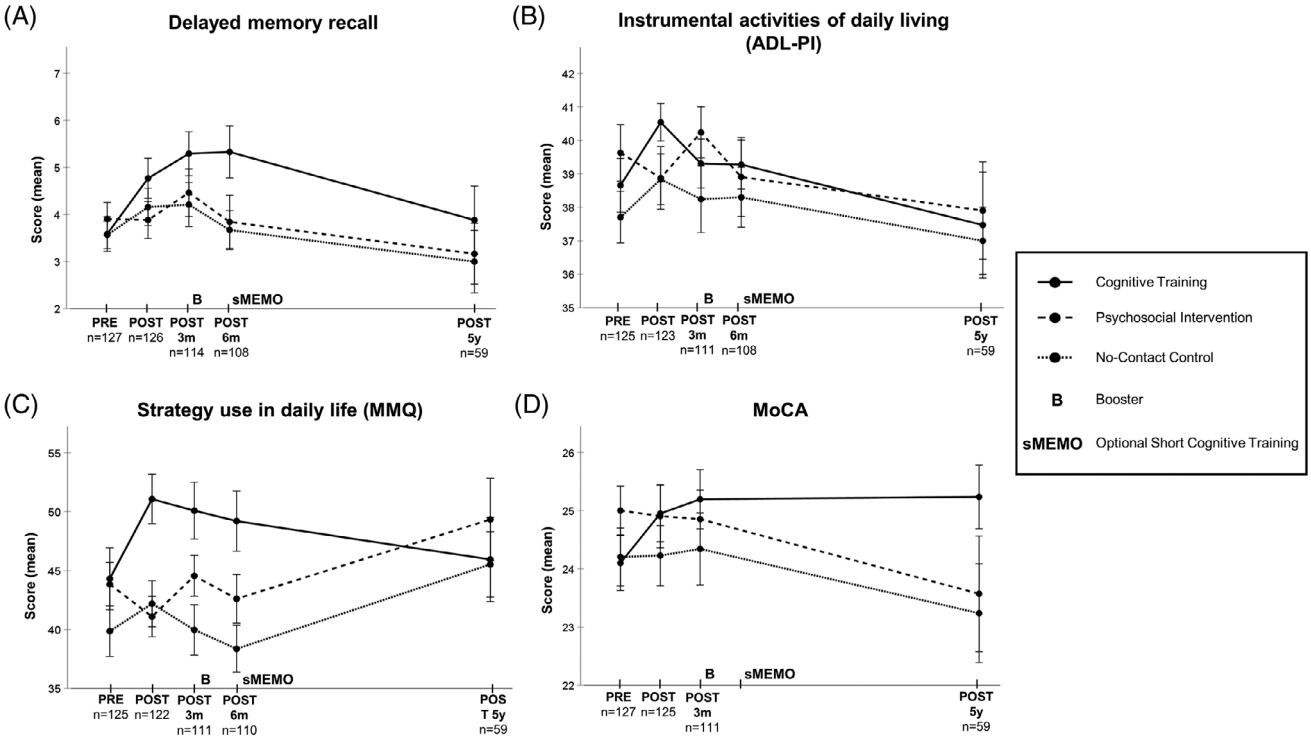

FIGURE 2 Outcome measures as a function of time and intervention group. Mean scores (±SEM) obtained on (A) delayed memory recall, (B) instrumental activities of daily living (ADL-PI), (C) strategy use in daily life (MMQ), and (D) MoCA. The number of participants who completed the test for a given outcome is indicated on the x-axis at each time point (PRE, POST, POST3m, POST6m, POST5y). The bold letter "B" indicates when the booster was provided (1 week following the 3-month assessment). The bold acronym "sMEMO" signifies when the short optional cognitive training was offered to participants from the psychosocial intervention and the no-contact group (about 1 year following the 6-month assessment). In (A), higher scores indicate better performance (range 0–12). In (B) and (C), higher scores indicate better self-reported ability to perform instrumental activities of daily living (range 0–45) and greater self-reported use of memory strategies in daily life (range 0–96), respectively. In (D), higher scores indicate better general cognitive performance (range 0–30). POST, post-intervention; POST3m, 3-month post-intervention; POST6m, 6-month post-intervention; POST5y, 5-year post-intervention; PRE, pre-intervention.

a significant effect of Group, $F(2,122.7) = 3.4$, $p = 0.04$, and Time X Group interaction $F(8,393.2) = 4.4$, $p < 0.001$. Compared with the no-contact group, cognitive training induced a significant improvement of the MMQ score from PRE to POST (mean change = 4.8, $p = 0.04$, d = 0.36, 95% CI [0.01,0.71]) and POST6m (mean change = 5.5, $p = 0.02$, d = 0.42, 95% CI [0.06, 0.78]), while the improvement was not significant at POST3m (mean change = 4.6, $p = 0.06$, d = 0.35, 95% CI [−0.02, 0.72]). However, the improvement observed in the cognitive training group compared to the control group was no longer found at POST5y (mean change = −3.2, $p = 0.30$, d = −.28, 95% CI [−0.80, 0.24]), as strategy use slightly decreased in the cognitive training group while it increased in the control groups. It is worth noting that no significant change was observed in the psychosocial intervention group from PRE to any POST time points, except for a decrease from PRE to POST (mean change = −5.0, $p = 0.03$, d = −0.38, 95% CI [−0.71, −0.04]). Furthermore, no significant change was observed from PRE to POST5y in the no-contact group.

A reliable improvement in MMQ was found in 29.4% of participants from the cognitive training group, while 29.4% of them experienced a decline. These percentages are not statistically different from those seen in the psychosocial intervention group (38.1% for both improvement and decline, $z = 0.6$, $p = 0.57$) and no-contact control group (28.6% for both improvement and decline, $z = 0.1$, $p = 0.96$) (Table 2).

3.5 | Clinical measure: MoCA

Figure 2D shows performance on the MoCA. The LMM showed no significant effect of Group, $F(2,124.8) = 1.5$, $p = 0.23$, but it did identify a significant effect of Time, $F(3,291.4) = 7.9$, $p < 0.001$, and a Group × Time interaction, $F(6,291.4) = 2.5$, $p = 0.02$.

When compared with the no-contact group, cognitive training exhibited no significant difference from PRE to POST ($p = 0.17$) and POST3m ($p = 0.18$). However, there was a significant increase from PRE to POST5y (mean change = 1.6, $p < 0.001$) with a large effect size (d = 0.96, 95% CI [0.43, 1.49]) (Table 2). In the psychosocial intervention group, no significant change was observed from PRE to any POST time points. As a reference, we observed a significant decrease of the MoCA score from PRE to POST5y in the no-contact group ($p < 0.001$; d = −0.74, 95% CI [−1.10, −0.38]).

The proportion of participants demonstrating reliable improvement on the MoCA at POST5y in the cognitive training group was 35.3%, a proportion that was not significantly different from that observed

TABLE 2 Effect of interventions on proximal and distal outcomes.

	Cognitive training	Psychosocial intervention (active control)	No-contact
Delayed memory recall (possible range 0–12)			
Mean score at baseline provided by the LMM (SD)	3.7 (2.5)	3.7 (2.5)	3.7 (2.5)
Mean change from PRE to POST5y[a]	1.6 ($p < 0.01$)	0.7	N/A[f]
Effect size relative to no-contact (95% CI)[b]	0.68 [0.22, 1.15]	0.29 [−0.17, 0.74]	N/A[f]
Reliable improvement %[c,d] (p for significance difference with cognitive training)	52.9	19.0 ($p < 0.05$)	19.0 ($p < 0.05$)
Reliable deterioration %[c,e]	23.5	28.6	47.6
Complex activities of daily living (possible range 0–45)			
Mean score at baseline provided by the LMM (SD)	38.9 (5.1)	39.4 (5.1)	37.6 (5.2)
Mean change from PRE to POST5y[a]	−1.1	−1.5	N/A[f]
Effect size relative to no-contact (95% CI)[b]	−0.18 [−0.55, 0.19]	−0.22 [−0.76, 0.32]	N/A[f]
Reliable improvement %[c,d]	18.8	9.5	28.6
Reliable deterioration %[c,e]	62.5	42.9	42.9
Strategy use in daily life (possible range 0–96)			
Mean score at baseline provided by the LMM (SD)	44.4 (13.3)	43.6 (12.9)	40.0 (13.3)
Mean change from PRE to POST5y[a]	−3.2	2.1	N/A[f]
Effect size relative to no-contact (95% CI)[b]	−0.25 [−0.72, 0.22]	0.17 [−0.29, 0.62]	N/A[f]
Reliable improvement %[c,d]	29.4	38.1	28.6
Reliable deterioration %[c,e]	29.4	38.1	28.6
MoCA (possible range 0–30)			
Mean score at baseline provided by the LMM (SD)	24.1 (3.3)	25.0 (3.3)	24.2 (3.3)
Mean change from PRE to POST5y[a]	3.0 ($p < 0.001$)	0.4	N/A[f]
Effect size relative to no-contact [95% CI][b]	0.96 [0.43, 1.49]	0.14 [−0.36, 0.65]	N/A[f]
Reliable improvement %[c,d]	35.3	23.8	14.3
Reliable deterioration %[c,e] (p for significance difference with cognitive training)	17.6	38.1	57.1 ($p = 0.02$)

Abbreviations: CI, confidence interval; LMM, linear mixed model; PRE, pre-intervention; POST5y, 5 years post-intervention; SD, standard deviation.
[a]Mean change from PRE to POST5y is defined as (group mean—control mean at POST5y)—(group mean—control mean at PRE).
[b]Positive effect size indicates improvement.
[c]p values are represented when significant differences were found between cognitive training, psychosocial intervention or no-contact condition.
[d]Calculated as the percentage of participants in each group who were ≥0.66 SEM.
[e]Calculated as the percentage of participants in each group who were ≤−0.66 SEM.
[f]The mean change from PRE to POST5y for the no-contact group is 0, as mean change is defined as (group mean—no-contact mean at POST5y)—(group mean—no-contact mean at PRE).

in both the psychosocial intervention group (23.8%, $z = 0.8$, $p = 0.44$) and no-contact group (14.3%, $z = 1.5$, $p = 0.13$) (Table 2). In the cognitive training group, a reliable deterioration of the MoCA score was observed in 17.6% of participants, a figure that was not significantly different from that observed in the psychosocial intervention group (38.1%, $z = 1.4$, $p = 0.17$), but lower than that measured in the no-contact group (57.1%, $z = 2.5$, $p = 0.01$).

4 | DISCUSSION

The aim of this study was to evaluate the 5-year impact of cognitive training in older adults with MCI. As anticipated, individuals with MCI exhibited declines in delayed memory, activities of daily living, and global cognition 5 years after the end of the intervention. Notably, an Intervention × Time interaction effect was observed for memory and global cognition: Participants who received cognitive training experienced a mitigated decline in memory, and their global cognition remained stable. We will now discuss each of these effects.

The LMM revealed a significant improvement in delayed memory performance from baseline to year 5 in the cognitive intervention group, with a medium effect size. Furthermore, the improvement in delayed memory recall observed 6 months after participants had completed cognitive training was still evident 5 years later. While there was a slight reduction in the cognitive training benefit at the 5-year mark, delayed memory remained higher than baseline in the cognitive

training group compared to the no-contact condition. None of these effects were observed following the psychosocial intervention, confirming that the long-term benefit is specifically attributable to the cognitive intervention. Additionally, a larger proportion of participants from the cognitive training group exhibited reliable improvement[16] in delayed memory from baseline to year 5, compared to the psychosocial and no-contact groups.

One remarkable finding in our study was the sustained maintenance of MoCA scores among participants in the cognitive training group over the 5-year period. The LMM indicated a significant increase in MoCA scores from baseline to year 5, with a large effect size. These results were not observed in participants from the psychosocial intervention group. Moreover, the cognitive training group demonstrated a significantly lower rate of reliable deterioration compared to the no-contact group, indicating reduced vulnerability to clinical decline in the former. While a few studies have shown post-training improvement in MoCA scores following cognitive or multimodal training in individuals with MCI,[28–32] none of them conducted follow-ups beyond 9 months post-intervention. Given the recognition of the MoCA as a clinical measure, these findings suggest that the cognitive training program may hold promise in delaying the progression of clinical symptoms. This underscores the potential of cognitive training as a preventive approach for cognitively vulnerable older adults, potentially delaying the onset of dementia.

As expected, individuals with MCI exhibited a significant decline in their self-reported ability to perform daily activities. Importantly, this decline was similar for both cognitive training and control groups, suggesting that cognitive training had no impact on this aspect. While we did not observe an effect at the 6-month mark as reported in our previous study,[5] we had anticipated that cognitive training might influence the increasing difficulties in performing complex daily tasks over the long-term follow-up. However, this expectation was not met. It is possible that the ADL-PI measure used here may not effectively capture the benefit of learned strategies or may lack sensitivity to subtle differences. Alternatively, the training benefit may not transfer to complex daily activities, which rely on multiple cognitive abilities and the context of use.[16,33]

The initial post-training increase in self-reported use of strategies in daily life was not maintained at year 5 when compared to the control conditions. This phenomenon could be attributed to an effect of the short version of MEMO program, which was offered for ethical reasons to participants randomized to the active or no-contact conditions. Interestingly, the MMQ scores of the part who received the short version of the cognitive training program appeared to increase from POST6m to POST5y (see Supplemental Materials S2).

The present study has several limitations. Our sample size was relatively small for the 5-year time point, with only 46.5% of the original sample completing the assessment. This lower participation rate may be attributed to the fact that the follow-up was not originally planned. Additionally, the decision to use a smaller set of tasks in comparison to the short-term study might have resulted in the exclusion of potentially valuable data. To optimize information content while minimizing participant burden, we focused on tasks that either displayed significance in the initial study (delayed memory, MMQ) or were anticipated to show decline during long-term follow-up (MoCA and ADL). For statistical reasons, the change values of the cognitive training group were only compared to the no-contact group. There is a possibility that individuals who did not return for the follow-up assessment experienced a greater decline compared to those who did. Finally, we offered a short version of the MEMO program to participants from the control conditions. While this did not result in an effect on delayed memory or the MoCA, it might have encouraged participants to use internal and external memory strategies.

In summary, this study is the first evidence of the enduring, long-term benefits of cognitive training on delayed memory recall and on a clinical global measure of cognition in individuals with MCI. The observed 5-year maintenance of these cognitive training effects is of paramount significance for managing MCI, a condition associated with declining autonomy and diminished quality of life. Furthermore, it is noteworthy that these enduring effects were achieved through a relatively brief, cost-effective intervention that can be readily implemented as a preventive measure for at-risk individuals.[34,35]

AUTHOR CONTRIBUTIONS

Sylvie Belleville: Study concept and methodology; funding acquisition; supervision; writing the first version of the manuscript. **Marc Cuesta**: Data curation; formal analyses; visualization; writing the first version of the manuscript. **Carol Hudon, Nathalie Bier, Catherine Brodeur, Chantal Viscogliosi, Serge Gauthier, Brigitte Gilbert, Marie-Christine Ouellet, and Sébastien Grenier**: Study concept and methodology; writing: review and editing.

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CONFLICT OF INTEREST STATEMENT

Sylvie Belleville has been a consultant for research development on the prevention of Alzheimer's disease for the Fondation IUGM (2016) and for Lucilab (2017 to current). She has also been involved in developing a cognitive stimulation program for the Centre de promotion de la Santé Avant Âge (2015). Sylvie Belleville holds intellectual property

rights for the "Programme de Stimulation pour une santé cognitive, Memoria, Batterie d'évaluation de la mémoire Côte-des-Neiges" and "MÉMO, Méthode d'Entrainement pour une Mémoire Optimale." Carol Hudon has worked as a rater in clinical trials (Lundbeck, Roche), and as a consultant for Bracket Global. Sébastien Grenier has intellectual property rights for the "Programme d'intervention psychosociale axé sur le bien être psychologique." Brigitte Gilbert served as a consultant for the development the "Ateliers de stimulation pour une santé cognitive" (2014). She also holds intellectual property rights for "MÉMO: Méthode d'entrainement pour une mémoire optimale" (2007). Marie-Christine Ouellet holds intellectual property rights for the "Programme d'intervention psychosociale axé sur le bien être psychologique." Chantal Viscogliosi is responsible for the training 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. Serge Gauthier is member of Scientific Advisory Boards with Alzheon, AmyriAD, Eisai Canada, EnigmaUSA, Lilly Canada, Medesis, Roche Canada, TauRx. Lectures for Biogen Canada, Lundbeck Korea. Nathalie Bier is responsible for training on occupational therapy assessment and interventions for adults and older adults with cognitive impairment at the Université de Montréal's continuing education training program. She is a founding member of a solidarity cooperative that sells technologies to support older adults aging in place. The other authors, Marc Cuesta and Catherine Brodeur, have no conflict of interest to disclose. Author disclosures are available in the Supporting Information.

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The sponsors were not involved in the design, methods, recruitment, data collection, analysis, or preparation of the paper.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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