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The benefits of cognitive training after a coronary artery bypass graft surgery

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Abstract Cognitive deficits are frequent after coronary artery bypass graft surgery (CABG) in the elderly population. In fact, memory and attention deficits can persist several months after the surgery. Recent studies with healthy older adults have shown that memory and attention can be improved through cognitive training programs. The present study examined whether memory training (method of loci and story generation) and attentional training (dual-task computerized training) could improve cognitive functions in patients aged 65 years and older who underwent CABG surgery. Participants (n = 51) were assigned to one of three groups: (1) control group (tested at 1, 3 and 6 months after the surgery), (2) attention training followed by memory training, (3) memory training followed by attention training (groups 2 and 3: tested at 1, 2, 3 and 6 months after the surgery). The trainings took place between the 6th and 10th week following the surgery. The three groups were compared before and after each training program using attention and memory tests and neuropsychological tests. The results showed that attention and memory trainings lead to significant improvement in the cognitive domain that was trained. It thus seems that cognitive training can be a promising tool to enhance cognitive functions after a CABG surgery.

Keywords Coronary artery bypass surgery · Cognitive training · Cognitive deficit

Introduction

The world's elderly population is currently 650 million and is expected to reach two billion by 2050 (World Health Organization, 2008). This has important implications for the health care system as seniors are generally more likely to be hospitalized than other age groups (United States Census Bureau, 2003). Cardiovascular disease is the main cause of mortality, for both men and women (World Health Organization, 2008). Due to advances in technology and growth of the elderly population, an increasing number of coronary artery bypass graft surgeries (CABG) are performed. In the United States, more than 425,000 patients undergo a CABG each year (American Heart Association, 2007). Studies have shown that CABG can be performed safely on the elderly population (e.g., Ascione et al., 2002). Although post surgery complication rates are acceptable, cognitive deficits after a CABG are common in older adults and they can persist several months after the surgery. The incidence of post surgery cognitive deficits varies between 25 and 80% (Funder et al., 2009). The short term incidence (less than 2 weeks after the surgery) varies between 30 and 80% and the long-term incidence (more than 1 month after the surgery) varies between 10 and 60% (Rasmussen,

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2006). This wide range of incidence is due to the variability in the study inclusion and exclusion criteria, the time interval of follow-ups, the specific neuropsychological battery employed, and the statistical criteria used to define cognitive decline (Selnes & McKhann, 2005). Also, an important limitation of most studies in this area is the use of non-specific and gross measures of cognitive and mental status, such as the Mini-Mental State Examination (Folstein et al., 1975), to assess cognitive deficits after surgery. Using more specific and sensitive measures of cognitive functions could enhance detection of cognitive deficits after CABG. These deficits severely impact on quality of life and reduce patient's involvement in a rehabilitation process (Barclay et al., 1988).

The aetiology of cerebral complications after CABG is multifactorial and different preoperative and operative factors may be associated with the cognitive deficits observed in some studies (Royter et al., 2005). The most generally accepted mechanisms responsible for cognitive dysfunction are intraoperative hypotension and multiple microembolization. In both situations, cerebral tissue hypoxia might result from these insults. A recent study reported a relationship between cerebral oxygen desaturation and postoperative cognitive dysfunction in elderly patients after CABG surgery (De Tournay-Jetté et al., 2011). Decline in sustained and selective attention are the most common cognitive deficits following CABG and can be observed within 10 days after surgery (Bruggemans et al., 1995; Knipp et al., 2004; Newman et al., 1995; O'Brien et al., 1992; Plourde et al., 1997; Shaw et al., 1986; Toner et al., 1998; Westaby et al., 2001). Deficits in immediate verbal memory have also been reported 10 days post surgery (Bruggemans et al., 1995; Knipp et al., 2004; Lee et al., 2003; Mora et al., 1996; Newman et al., 1995; Plourde et al., 1997; Shaw et al., 1986; Westaby et al., 2001).

In recent studies including healthy older adults, is has been shown that cognitive training can enhanced cognitive performances in memory and attention tasks, suggesting that cognitive plasticity is possible even in advanced age (Baltes & Kliegl, 1992; Bherer et al., 2008; Cavallini et al., 2003; Ho & Scialfa, 2002; Verhaeghen et al., 1992). In cognitive training interventions, participants engage in substantial practice using computerized tasks designed to target a specific cognitive function. Individualized feedback is often used to maximize training benefits. Typically, training effects in older and younger adults are quantified by contrast with test–retest improvement observed in control groups that did not receive any training. Some cognitive training studies have reported an equivalent training benefit for younger and older adults (Bherer et al., 2008; Cavallini et al., 2003; Ho & Scialfa, 2002), some a reduced benefit for older adults (Baltes & Kliegl, 1992; Verhaeghen et al., 1992), and others a greater benefit for older compared to younger adults (Bherer et al., 2008; Kramer et al., 1995). Together, all these studies suggest that healthy older adults can benefit from cognitive training.

Thus far, laboratory based cognitive training studies have shown positive results in improving attentional control in older adults. However, evidence for transfer effect to non-trained tasks remains limited. The transfer effects are important to show that training-induced improvements entailed more than specific learning of stimulus–response mappings (Batsakes & Fisk, 2000). Many previous studies have found narrow transfer after cognitive training (e.g., Ball et al., 2002). However, other studies in the literature suggest transfer of training after attention training (Bherer et al., 2005; 2008; Kramer et al., 1995). Using a processing speed training program, Edwards et al. (2002, 2005) and Roenker et al. (2003) obtained transfer effects with everyday speed measures (Timed Instrumental Activities of Daily Living; the Road Sign Test; on-the-road driving performance), but reported limited transfer effect in clinical neuropsychological tests. More recently, Jaeggi et al. (2008) reported a significant improvement in fluid intelligence after training with a demanding working memory task, and the training effect was dosage-dependent. In another study, Buschkuehl et al. (2008) showed transfer effects in memory tasks after a working memory training in older adults, which suggests that brain plasticity can lead to transfer effects even in advanced age (see also Zelinski, 2009). In the present study, transfer effects were assessed through correlation analyses between improvement observed in the training tasks and changes indexed in clinical tests of memory and attention.

To our knowledge, cognitive training has never been used to improve cognition in a cardiac population of older adults after CABG. The aim of this study was to assess the efficacy of attentional training (dual-task computerized training) and memory training (method of loci and story generation) to enhance cognitive function in patients aged 65 years and older who underwent CABG surgery. Given the important inter-individual variability in post-operative cognitive decline, the present study was designed to minimize variability among patients by using specific inclusion/exclusion criteria, assessments at several time intervals, including a 6 month follow-up, and using a specific neuropsychological test battery that assesses cognitive abilities typically found to decline after CABG surgery (i.e., attention and episodic memory). In line with the existing literature, we expected (1) significant cognitive decline in attention and memory after CABG surgery, (2) specific improvement in attention performances after attention training and in memory scores after memory training in the training groups, (3) general improvement in attention and memory in the training groups compared to the control group, and (4) significant gains in neuropsychological tests of attention and memory in the training groups.

Methods

Participants

Between January 2006 and March 2008, 51 patients were enrolled in this study. Patients were recruited from specialized cardiology hospitals from the Montreal area. Patients were included if they were 65 years or older and were scheduled for a first CABG surgery without concomitant surgery. Exclusion criteria involved history or current drug or alcohol abuse, psychotic disorder, neurological disease (including having a stroke), or a prescription of antidepressants or lithium. Also, patients were excluded if the Mini-Mental State Examination score prior to surgery was <24. Mini-Mental State Examination was administered by a trained research assistant and other exclusion criteria were evaluated from the patient's medical record. Of the 51 patients who had started the cognitive training program 1 month after the surgery, a total of 44 patients completed the study (see Fig. 1).

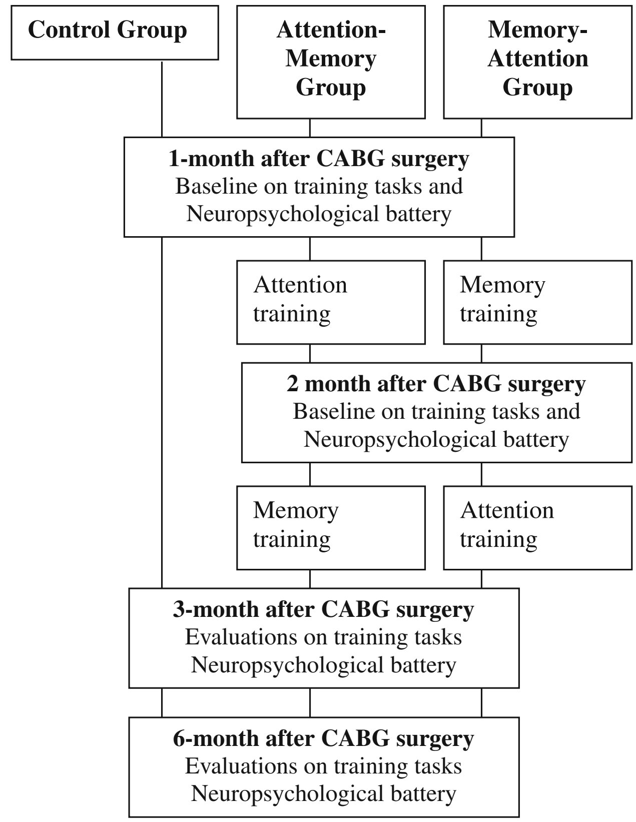

Fig. 1 Study design

Neuropsychological assessment

The neuropsychological battery included six tests that have been shown to be sensitive to cognitive changes following cardiac surgery (Pugsley et al., 1994) and that can be performed in the limited time available the day prior the surgery. All neuropsychological assessments and training sessions were conducted by trained research assistants. The training of the research assistants took an average of 60 h and they were supervised throughout the project. The following tests were used: Mini-Mental State Examination, Logical Memory Subtest of the Rivermead battery (with three alternatives stories for each time of testing), Rey Auditory Verbal Learning Test (RAVLT) (three alternatives versions for each time of testing), the digit symbol of the Wechsler Adult Intelligence Scale-revised (WAIS-R), the Trail Making Test (TMT) part A and B, the Stroop Test, and the Verbal Fluency Test (three alternatives versions for each time of testing). The Mini-Mental State Examination was used only before surgery to determine the eligibility of the patient in the study. All the other tests were completed at each of the three neuropsychological assessments.

Mini-Mental State Examination is a test of neurocognitive functions such as orientation (i.e., *date, emplacement of evaluation*), attention and calculation (i.e., 100-7…), memory (encoding and recalling three words), and language (naming object and writing a sentence). According to Strauss et al. (2006), the internal consistency of this test is .96, the inter-judge reliability is .65, and test–retest stability for intervals of less than 2 months varies between .80 and .95.

The Logical Memory Subtest of the Rivermead battery was used to examine the immediate and delayed memory as well as the recovery capacity. In this test, participants are asked to recalls a story read aloud by the examiner, both immediately and after a delay. A yes/no recognition test follows the delayed recall. According to Strauss et al. (2006), inter-judge reliability is very high and may be close to 100%.

The RAVLT examined learning, immediate and delayed memory, recovery capacity and interference effect. This test affords an analysis of learning and retention using a five–trial presentation of a 15-word list (list A), a single presentation of an interference list (list B), two post-interference recall trials (one immediate, one delayed), and recognition of the target words presented with distracters (Lezak et al., 2004). According to Strauss et al. (2006), the test–retest reliability over a 1-year interval varies between .60 and .70.

The digit symbol of the WAIS-R was used to assess psychomotor speed and sustained attention. In this test, nine digit-symbols are paired and are followed by a list of digits. Participants are asked to copy the corresponding symbol as fast as possible. Participant's score corresponds to the number of symbols correctly drawn within 120 s (Wechsler, 1997). According to Franzen et al. (1989), the test–retest reliability over an interval of 2–7 weeks is .69.

The Trail Making Test assessed attention (part A & B), complex visual-motor coordination and attentional switching (part B). In the Trail Making Test part A, participants are asked to draw a line between 25 numbers in ascending order as fast as possible. In the Trail Making Test part B, participants have to draw a line alternatively between letters (from A to L) and numbers (from 1 to 13) (Reitan, 1958). According to Strauss et al. (2006), test–retest reliability in older adults over a 1-year interval may vary between .53 and .64 for part A and is somewhat higher for part B (0.67–0.72).

The Victoria Stroop Test assessed selective attention and inhibition. This test includes three cards, each of which contains six rows of four items. Within each row, one item is presented in each of the following colors: red, blue, yellow, and green. On each of the three tasks, participants are asked to name the color of items as quickly and accurately as possible. On the first part, the Dot task, items are colored dots. On the second part, the Neutral Word task, the items are common words (i.e., *when, hard, and, over*). On the third and final part, the Color Word task, the items are color names (i.e., red, blue, yellow, green) printed in color not corresponding to the word themselves (Troyer et al., 2006). According to Strauss et al. (2006), test–retest reliability over a 1-month interval is high and may reach .90 for the first part, .83 for the second part, and .91 for the third part.

Finally, the Verbal Fluency Test assessed executive functions. In this test, participants are asked to generate as many words as they can that begin with a specific letter (e.g., *P–T-L*), within 90 s. According to Strauss et al. (2006), test–retest reliability is high and may reach .70 for short (e.g., 1 week) as well as long (e.g., 5 years) intervals.

Attention training task

The dual-task training used in this study has been used successfully to improve divided attention in healthy older adults (Bherer et al., 2005). In this task, participants performed two discrimination tasks (visual and auditory) individually (single task) or concurrently (dual task: both visual and auditory). In the visual task, the letters (B or C) appeared in white on a black background and participants had to respond with one key for B and another key for C. In the auditory task, participants discriminated between a low tone and a high tone pitch (440 Hz vs. 990 Hz; duration = 250 ms) delivered through headphones equipped with a volume control. Similar to the visual task, one key was pressed for a high tone and another key for a low tone.

Training involved pure blocks (single task trials: only one of the two tasks was performed) and mixed blocks (single mixed and dual mixed). A pure block contained 20 single-task trials (10 of each stimulus). The mixed blocks were composed of 40 single-task trials (20 visual and 20 auditory: single mixed) and 40 dual-task trials (dual mixed). The order of the single-mixed and dual-mixed trials was randomized. In the pre and post-training assessments, participants completed two pure blocks (one visual one auditory) followed by two mixed blocks. In each training session, they completed two pure blocks followed by eight mixed blocks. Instructions emphasized response speed and accuracy.

At pre- and post-assessments, no feedback was presented for speed, but incorrect responses were indicated by a message ("wrong answer") appearing in red in the middle of the screen. During the training sessions, individualized performance feedback was provided. The feedback took the form of an odometer presented on the top left part on the computer screen. The needle of the odometer moved according to response speed and the color of the odometer (red, yellow, green) indicated to the participant whether the performance was slower, faster or equal to the mean reaction time of the last 5 trials in a pure block divided by a ratio of 1.8. In the mixed blocks, the feedback depended on the ratio of the dual-mixed trials on the single-mixed trials and was intended to help participants to achieve a level of performance in dual-task trials close to the one obtained in single-task trials. Therefore, the odometer appeared in red (slow performance) when the mean reaction time for the last 5 dual-mixed trials was larger or equal to the mean reaction time of the single-mixed trials multiplied by a ratio of 3.6. It appeared in green (good performance) when the mean reaction time for the last 5 dual-mixed trials was smaller or equal to the mean reaction time of the single-mixed trials multiplied by a ratio of 1.6. The odometer appeared yellow when performance fell between these two criteria.

Memory training task

In the memory training task, participants learned to use two different memory strategies; the method of loci and self-generated stories. Participants were presented with word lists (containing 15 words each) to memorize and were provided with memory strategies that were explained by the trained research assistant. For the method of loci, the participants were told to create a mental map of some familiar locations in their home and then imagine each target word from the list in one of these familiar locations. The software program proposed four locations: kitchen, living room, bedroom and washroom. In each of these locations, there was some specific position where it was possible to put an object (e.g., refrigerator, table, coach, etc.). Locations' names remained on the computer screen during testing and could be used as clues for remembering target words. For the self-generated stories strategy, participants were asked to integrate each word in a story that they generated spontaneously.

At each assessment time (pre-training, training, and post-training) strategies were practiced and then target words were presented successively in a box at the bottom of the screen. A total of 16 lists were available and eight of them were used for the pre and post assessments. The eight remaining lists were used for training sessions. Each of these lists was used twice, never in the same session, and never with the same learning strategies. Time presentation of the stimuli was 3 s for the method of loci and 4 s for the self-generated stories strategy. The number of lists was greater in training sessions (two lists for each strategy) versus pre and post assessments (one list for each strategy) and during training sessions the experimenter provided tips and examples to facilitate the use of the memory strategies.

After the presentation of an entire list, the participant recalled words using a memory strategy and wrote them down on a white sheet. The method of loci was always the first strategy to be assessed. The number of words correctly recalled was calculated for each trial. The experimenter ensured the use of memory strategies by asking participants to provide the location of each word for the method of loci and by asking the participant to repeat the story aloud for the self-generated stories.

Procedure

Participants were assigned to one of three cohorts. Since double-blind could not be preserved, a cohort design was preferred to a randomisation design to avoid a negative expectation effect in the control group. Recruitment lasted 26 months. In order to ensure that each cohort had a minimal number of patients that completed the trial at the same time over the 2-year periods, thus avoiding seasonal effects [i.e., potential effects of changes at the health care center or in medical staff) between participants of a given cohort, two patients from each cohort were randomly assigned to one of the three experimental conditions (control group, attention training followed by memory training (A-M), memory training followed by attention training (M-A)]. Assignment followed a randomization schedule generated by a computer. To ensure that differences between groups would not be due to negative expectations, participants of the control group were not informed of the two experimental groups and were given a different consent form.

All patients completed a neuropsychological assessment the day prior to surgery and 3–10 days after, usually a day after leaving the intensive care unit. During the first assessment, which lasted between 30 and 45 min, they also answered questions about their health, demographic information, psychological distress and subjective cognitive functioning. Information was also gathered from patients' medical chart (medication). One month after the surgery, all patients completed the same neuropsychological battery and were tested on the attention and the memory training tasks used for training. The 1-month post-surgery assessment is used as baseline prior to the intervention (see Fig. 1 for the study design). Between the sixth and the eighth week after the surgery, the first part of the training took place; the A-M group completed the attentional training, while the M-A group did the memory training. Each of the cognitive training was composed of four training sessions and the frequency of training sessions was twice a week. Each training session lasted approximately 50 min. After the first part of the training, the two experimental groups were assessed again with the neuropsychological battery and the experimental tasks (attention and memory). Between the eighth and tenth week, the second part of the training took place (memory training for the A-M group and attentional training for the M-A group). Finally, the three groups of patients were assessed three and sixth months after surgery with the neuropsychological battery and the attention and memory training tasks.

Statistical analyses

First, an analysis of variance (ANOVA) was conducted prior to CABG surgery to assess baseline differences in demographics, baseline neuropsychological test results, and intra-operative data. To test the first hypothesis (cognitive decline after surgery), postoperative cognitive deficit was defined as a drop of one standard deviation (SD) on two or more neuropsychological tests from the preoperative evaluation and the first postoperative evaluation. According to Mahanna et al. (1996), this criterion is the most frequently used index to define decline.

To test the second hypothesis, that the attention and memory training programs will lead to specific training gains, repeated ANOVAs were performed separately on attention and memory scores with groups as between subject factor (M-A vs. A-M) and assessments time as within-subject factor (1, 2 and 3 months after surgery). When significant, interactions were analysed by examining simple effects or repeated-contrasts if the interaction involved more than two levels of a repeated factor (e.g., three assessment times). At the 2-month assessment, the M-A group had only received memory training and the A-M group had only received attentional training. At

3 month, both groups had received both types of training. The dependent variables of interest in the attention task were reaction time and accuracy. Reaction time was calculated from stimulus onset to the participant's response. Trials were not included in the analyses when an incorrect response was produced or when reaction time was longer than 5,000 ms or shorter than 100 ms. Accuracy data corresponded to the percentage of correct answers in each condition. The dependent variable of interest in the memory task was the number of words recalled. Analyses were performed using the total number of words recalled after five trials (maximum of 75 words).

To test the third hypothesis (patients who received training would outperform controls), performances on the attention and memory tasks were pooled for the two training groups and compared to control participants. Repeated ANOVAs were performed with groups as between subject factor (training vs. control) and assessments time as within-subject factor (1, 3 and 6 months after the surgery).

To test the fourth hypothesis that the benefits of training would transfer to clinical measures, ANCOVAs were performed on neuropsychological test scores with one between-subjects factor (training vs. control) and one within-subjects factor (1, 3 and 6 months assessments), while controlling for school education level (covariate). When a group $\times$ assessment interaction reached significant level, the linear and quadratic trends were tested in each group. A linear trend reflects difference between groups in changes from the first month to the sixth, whereas a quadratic trend reflects a difference between groups in the comparison between the third month (end of training) and the first and sixth pooled. Univariate correlations were also performed between the improvements observed on the computerized tasks and the improvements observed in neuropsychological assessments for trained groups.

All analyses were performed using SPSS software for windows (SPSS 15.0, SPSS Inc., Chicago, IL, USA). A P value (two-tailed) below 0.05 was considered to be statistically significant. When Mauchly's test of sphericity indicated violation of homogeneity of variance, adjusted alpha levels were used with Greenhouse-Geisser correction coefficient.

Results

Pre-operative baseline and pre-training data

The preoperative neuropsychological testing was performed the day prior the CABG surgery. On average ($\pm$SD), the first postoperative neuropsychological testing was performed 5.35 ± 2.73 days after CABG, and the 1-month neuropsychological testing was done 38.39 ± 6.04 days after surgery. Finally the 3 and 6 month neuropsychological assessments were done respectively, 98.02 ± 6.88 and 191.28 ± 8.91 days, after surgery. ANOVAs performed at baseline revealed that the three groups of patients and the drop-out group were comparable for demographics, clinical and intra operative data (see Table 1). The groups were also comparable on all neuropsychological tests at 1 month (used as baseline before cognitive training). Four participants dropped-out during the cognitive training and three did not complete the last evaluation. Three of them were in the control group, two in

Table 1 Demographics and medical variables for each group

Variables	Control group	A-M group	M-A group	Drop-out patients
Sample size	18	13	13	7
Age				
M	70.89	69.92	70.85	71.00
SD	4.44	3.93	4.51	5.20
Scolarity (y)				
M	10.78	9.58	10.31	13.58
SD	5.23	3.7	3.59	4.20
Sex				
Female n (%)	1 (5.6)	3 (23.1)	5 (38.5)	1 (14.3)
Male n (%)	17 (94.4)	10 (76.9)	8 (61.5)	6 (85.7)
Clinical variables				
BMI				
M	27.50	28.87	28.19	26.40
SD	3.54	4.02	4.73	2.11
Diabetes, n (%)	5 (27.8)	4 (30.8)	4 (30.8)	3 (57.1)
Hypertension, n (%)	11 (61.1)	10 (76.9)	10 (76.9)	5 (71.4)
Dyslipidemi,a n (%)	12 (66.7)	9 (69.2)	10 (76.9)	5 (71.4)
Angina Pectoris, n (%)	14 (77.8)	9 (69.2)	9 (69.2)	3 (85.7)
Heart failure, n (%)	2 (11.1)	3 (23.1)	2 (15.4)	1 (14.3)
Intraoperative parameters				
Duration of ECC (min)				
M	42.14	71.80	60	64.20
SD	33.76	29.99	33.95	36.89
Cross clamp time (min)				
M	42.67	43.70	34.6	41.00
SD	45.25	27.44	17.39	20.08
Postoperative outcomes				
ICU (days)				
M	4.94	4.45	4	5.43
SD	1.52	2.07	1.47	2.99
Total LOS (days)				
M	8.82	9.50	9.30	9.14
SD	3.48	2.75	4.59	2.41

BMI body mass index, *ECC* extracorporeal circulation, *ICU* intensive care unit, *LOS* length of stay, *SD* standard deviation

Table 2 Mean reaction times (ms) for each group in the dual-task

	Control group ($n = 18$)						Attention-memory group ($n = 13$)						Memory-attention group ($n = 13$)					
	1 month		3 months		6 months		1 month		3 months		6 months		1 month		3 months		6 months	
	M	SD	*M*	SD	*M*	SD	*M*	SD	*M*	SD	*M*	SD	*M*	SD	*M*	SD	*M*	SD
Single pure	1,042	88	989	42	984	47	1,085	101	823	48	918	55	1,047	102	794	49	960	55
Single mixed	1,850	96	1,746	60	1,728	63	1,598	110	1,172	68	1,414	72	1,722	110	1,015	68	1,307	72
Dual mixed	2,344	119	2,258	72	2,108	76	2,363	136	1,523	82	1836,	86	2,266	136	1,380	83	1,706	87

the A-M group and two in the M-A group. Intent-to-treat analysis performed with the data available for these 7 patients did not modify any of the results reported (Table 2).

Hypothesis 1: Cognitive decline in attention and memory after CABG surgery

The first hypothesis was supported as 68% of the sample showed a postoperative cognitive decline. The most sensitive tests were the number of words recalled for the Rey Auditory Verbal Learning Test (47% of patients showed a decline), Verbal Fluency (40% of patients showed a decline) and the Digit Symbol subtest of the WAIS-R (29% showed a decline). One month after the surgery, 19 (41%) patients still showed a cognitive decline. Three months post CABG, only six patients (14%) showed a cognitive decline. Three of them were in the control group, two in the A-M group and one in the M-A group.

Hypothesis 2: Specific improvement in attention performances after attention training and in memory scores after memory training

In the attentional training program, the specificity of training was verified with repeated ANOVAs involving one between-subjects factor (A-M group and M-A group) and three within-subject factors: task (visual and auditory), assessment times (1, 2 and 3 months after surgery) and trial types (single pure, single mixed, and dual mixed). There was no main effect of task (visual vs. audio) or interaction involving this factor in reaction time and Accuracy (all *F*, n.s.) and therefore in the results presented here, data were pooled for the two tasks. Figure 2 (upper panel) presents mean reaction time observed in the attention task. The results indicated a Time × Group interaction, $F(1.55, 37.14) = 11.20$, $P < .001$, $\eta^2 = .32$, due to a larger improvement in the A-M group between the first and the second month (588 ms) as compared to the improvement observed in the M-A group (161 ms). Moreover, a significant Time × Condition × Group interaction, $F(2.77, 66.43) = 4.39$, $P < .01$, $\eta^2 = .16$, was observed due to a

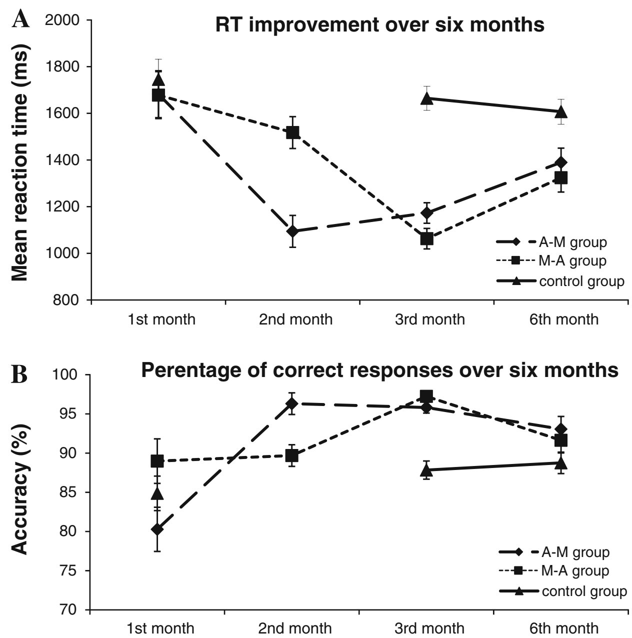

Fig. 2 Mean reaction time in milliseconds (**a**) and percentage of correct responses (**b**) for the Memory-Attention (M-A), the Attention-Memory (A-M) and the control groups at 1, 2, 3, and 6 months after the surgery

significantly larger improvement between the first 2 months in the dual-mixed trials (from 2,363 to 1,405 ms) compared to the single-mixed trials (from 1,598 to 1,098 ms) in the A-M group, $F(1, 12) = 28.21$, $P < .001$, $\eta^2 = .70$. This effect was not observed in the M-A group $F(1, 12) = .37$, $P =$ n.s., $\eta^2 = .03$. There was no difference between single-mixed trials and single-pure trials at 2 months for both the A-M, $F(1, 12) = 2.99$, $P =$ n.s., $\eta^2 = .20$, and the M-A, $F(1, 12) = 3.31$, $P =$ n.s., $\eta^2 = .22$, groups.

A similar pattern of results was observed in accuracy (see Fig. 2). A significant Time × Group interaction, $F(1.28, 24) = 10.77, P < .001, \eta^2 = .31$, indicated a larger improvement for the A-M group (16%) as compared to the M-A group (0.7%) at the 2 month assessment. A significant Time × Condition × Group interaction, $F(1.96, 46.99) = 5.65$, $P < .01$, $\eta^2 = .19$, also revealed a larger improvement in dual-mixed trials compared to single-mixed trials in the A-M group between the first 2 months, $F(1, 12) = 18.90$, $P < .001.$, $\eta^2 = .61$, which was not observed in the M-A group $F(1, 12) = 1.49$, $P =$ n.s., $\eta^2 = .11$. There was no difference between single-mixed and single-pure trials in both the A-M, $F(1, 12) = .61$, $P =$ n.s., $\eta^2 = .05$, and the M-A, $F(1, 12) = .46$, $P =$ n.s., $\eta^2 = .04$, groups. In sum, both reaction time and accuracy results suggest that the attentional training had a specificity effect. At 2 months, the A-M group exhibited better performances and became more efficient at executing the two tasks at the same time than the M-A group. At 3 months, when both groups had completed the attention training, there was no longer a difference between the groups in attentional performances.

In the memory tasks, ANOVAs were performed separately for each memory task (method of loci and self-generated stories) with Group as a between-subjects factor (A-M vs. M-A) and Assessment times as a within-subject factor (1, 2 and 3 months assessment). Results showed a significant Time × Group interaction with the Method of loci, $F(2, 48) = 3.97$, $P < .05$, $\eta^2 = .14$ (see Fig. 3). One-way ANOVAs comparing groups at each follow-up assessment, revealed that the difference between groups appeared only at the second month assessment, $F(1, 25) = 4.02$, $P < .05$, where the mean number of words recalled was higher (47 words) for the M-A group than the A-M group (36 words). When both groups had received the memory training (third month assessment), performances were equivalent in both groups, $F(1, 25) = .67$, $P =$ n.s. Results obtained with the self-generated stories method (see Fig. 3) showed a main effect of Time assessment, $F(1.24, 29.75) = 18.83$, $P < .001$, $\eta^2 = .44$, due to an increase in the number of words recalled between the first (38 words) and the second (51 words) assessment, $F(1, 24) = 11.24$, $P < .01$, $\eta^2 = .32$, and between the second and the third (57 words) assessment, $F(1, 24) = 18.08$, $P < .001$, $\eta^2 = .43$. However, the improvement observed with the self-generated story recall strategy was equivalent in both groups as indicated by the absence of a Group × Time interaction, $F(1.24, 29.75) = .42$, $P =$ n.s., $\eta^2 = .02$.

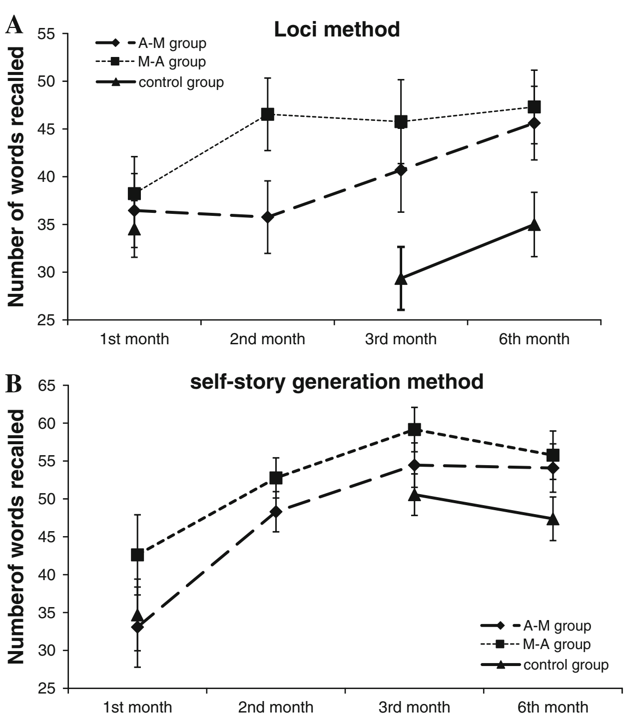

Fig. 3 Total of words recalled after five trials with the loci method (**a**) and the self-generated stories method (**b**) for the Memory-Attention (M-A), the Attention-Memory (A-M) and the control groups at 1, 2, 3, and 6 months after the surgery

Hypothesis 3: General improvement in attention and memory in the training groups compared to the control group

Previous analyses showed that performances were equivalent among training groups after completion of the two training programs and therefore the data of the two training groups were pooled to assess training effects compared to test–retest effect observed in control participants. An ANOVA comparing group (control vs. experimental), and Assessment times (1-, 3-, 6-month assessment) was conducted for each task (attention and memory) and each measure (reaction time and accuracy). For the attention task, a significant Time × Group interaction in reaction time, $F(1.58, 65.01) = 12.57$, $P < .001$, $\eta^2 = .24$, was observed, such that between the first and third month, reaction time of the control group only decreased by 81 ms in comparison with a 562 ms decrease in reaction time for the training group. Between the third and sixth month evaluation, reaction time of the control group decreased by 57 ms whereas it decreased in the experimental group by 238 ms. A similar pattern was found for accuracy, with a significant Time × Group interaction, $F(1.61, 67.76) = 5.57$, $P < .009$, $\eta^2 = .12$. Again, between the first and third month, performances increased by 4% in the control group compared with a 12% improvement in the experimental group. Between the 3-month and the 6- month assessment, accuracy increased by 1% in the control group and decreased by 4% in the experimental group.

In the memory tasks, results obtained with the Method of loci showed a Time × Group interaction, $F(2, 82) = 7.16$, $P < .001$, $\eta^2 = .15$. The total number of words recalled by the control group between the first and third month dropped from 35 to 29 words, whereas it increased from 37 to 43 words in the experimental group (see Fig. 3). In the self-generated stories task, there was a significant main effect of assessment time, $F(1.33, 53.13) = 27.65$,

$P < .001$, $\eta^2 = .41$, due to an increase in words recalled between the first month (35 words) and the third month (51 words), $F(1, 40) = 39.50$, $P < .001$, $\eta^2 = .50$, but not between the third month (51 words) and the sixth month (47 words) $F(1, 40) = 3.25$, $P =$ n.s., $\eta^2 = .08$. This was equivalent in all groups since the interaction with group was not significant, $F(1.33, 53.13) = .40$, $P =$ n.s., $\eta^2 = .01$.

Hypothesis 4: Significant gains in neuropsychological tests of attention and memory

ANCOVAs were performed on neuropsychological test scores with group as a between-subjects factor (control vs. experimental) and one within-subjects factor (first, third and sixth month assessments), while controlling for school education level (covariate). A Group × Time interaction was found in the quadratic trend for the digit symbol, $F(1, 41) = 6.00$, $P < .05$, $\eta^2 = .13$, as well as for the inhibition condition of the Stroop test (Stroop 3 in Table 3), $F(1, 39) = 4.19$, $P < .05$, $\eta^2 = .10$. Indeed, experimental groups showed greater improvements after cognitive training in comparison to the control group. A significant linear trend indicated differential improvement between groups for several subtests of the RAVLT: the immediate recall after the interference list, $F(1, 41) = 12.09$, $P < .001$, $\eta^2 = .23$, the delayed recall, $F(1, 41) = 8.46$, $P < .01$, $\eta^2 = .17$, and the number of false recognitions $F(1, 41) = 5.15$, $P < .03$, $\eta^2 = .11$. For each subtest, the performance of the control group did not change over time while the performance of the experimental groups improved.

Univariate correlation analyses were performed to assess the relationship between improvements observed on the computerized tasks and on the neuropsychological tests in participants that completed the training (M-A + A-M, N = 26). For the divided attention task, a global reaction time score was computed based on the average reaction time from the three types of trials (single-pure, single mixed and dual-mixed). Improvement scores were computed by subtracting mean global reaction time score at the third month from the mean global reaction time at the first month. An improvement score was also computed for each neuropsychological test. The improvement observed in reaction time after attention training was significantly correlated with improvement in the Trail making test part B ($r = .34$, $P < .05$), and was marginally correlated with the improvement in the Digit Symbol test($r = -.28$, $P = .07$). In the memory task, significant correlations were observed between the improvement in the number of words recalled using the method of loci and the improvement in the Digit Symbol test, $r = .29$, $P < .05$. The improvement in words recall observed with the self-generated stories task was correlated with changes in the immediate recall ($r = .36$, $P < .05$) and the delay recall of the Rivermead test ($r = . 34$, $P < .05$) and with the inhibition condition of the Stroop test ($r = -.44$, $P < .01$) 3 months after the surgery.

Discussion

Results of the present study suggest that older adults who underwent a CABG are likely to show post-operative cognitive deficits that can last several weeks and months post-surgery. However, the results also showed that these patients could benefit from a cognitive training program designed to improve performances on attention and memory tasks. The first major finding of the present study is that after a CABG surgery, 65% of the patients showed an early postoperative cognitive deficit 1 week after the surgery, and 41.3% still showed a postoperative cognitive deficit 1 month after the surgery. This result is consistent with some studies on incidence of postoperative cognitive deficit (Grote et al., 1992; Rasmussen et al., 2001) but others have reported higher prevalence in elderly population (Murkin et al., 1995; Newman et al., 1993).

This study also demonstrated the specific effects of cognitive training. Participants showed improvement in the

Table 3 Scores on neuropsychological tests for which the Group × Time interaction was significant

Neuropsychological test	Control group						Experimental groups					
	1 month		3 months		6 months		1 month		3 months		6 months	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Digit symbol	47.06	11.66	49.17	8.72	50.33	8.52	50.58	13.46	56.08	13.61	54.54	12.68
Stroop 3	34.44	10.83	33.93	8.53	32.72	7.64	36.73	11.16	31.94	10.25	34.49	14.47
RAVLT_recall after interference list	6.17	2.48	7.61	3.07	5.94	2.80	6.38	2.89	8.12	2.75	8.65	2.97
RAVLT-delayed recall	5.67	2.99	7.44	3.07	5.89	2.70	5.77	3.14	8.27	2.95	8.31	2.43
RAVLT-false recovery	6.89	5.01	5.78	3.77	7.50	4.48	5.15	4.60	4.38	4.75	2.65	3.62

RAVLT rey auditory verbal learning test, *SD* standard deviation attention task only after they received the attention training, with larger improvements in dual-task compared to single task performances. This suggests that dual-task training leads to enhanced divided-attention and a better ability to coordinate the execution of multiple tasks. The effect of memory training with the method of loci task was also specific to memory performances. However, the self-generated stories task did not show specific training effects, as all participants showed spontaneous improvements as early as the first assessment time.

A third important finding of the present study was that those who received cognitive training showed significant improvements in performance compared to the control group. These observations are in line with studies that showed a positive effect of attention training (Bherer et al., 2008) and memory training (Cavallini et al., 2003) in healthy older adults. Moreover, the improvements observed with training were correlated with improvements in some neuropsychological tests that have shown cognitive decline in CABG patients. Improvements in reaction time observed after attention training was significantly correlated with changes in the Trail making test part B and was marginally correlated with the Digit Symbol subtest of the WAIS-R. Moreover, improvements observed in the immediate and the delayed recall of the Rivermead Test correlated with changes in performances in the self-generated stories task. The improvements in the inhibition condition of the Stroop test correlated with improvements in the self-generated stories task. These results suggest that cognitive plasticity induced by the training tasks was strong enough to result in performance increases in tasks that were not trained during the intervention.

Taken together, these results suggest that cognitive training can be a useful rehabilitation tool in CABG patients that show post-operative cognitive decline. This study had multiple strengths. The research design allowed participants to benefit from the two cognitive trainings and to examine the specificity of the training by analysing order effects. There was also a follow-up at 6 months after the surgery, which revealed that training benefits were maintained over time. The present study also had some limitations. For instance, it would be interesting to extend the follow-up at 1 year in future research. Further studies with a larger sample size are also needed to support the present findings. Another limitation of the present study is that multiple neuropsychological evaluations were performed. Although alternative versions of tests were used when available, test–retest effects likely impact on the data. It is important to note however, that comparisons that involved the control group partially control for the test–retest effect.

Results of this study might have a significant impact on cognitive rehabilitation after CABG. Many studies have shown that cognitive deficits can follow CABG surgery and that decline can persist months and years following the surgery. Such decline can severely impair patients' quality of life. Moreover, the increasing number of older adults in cardiac population will likely increase the likelihood of cognitive deficits. Therefore, there is an urgent need to develop rehabilitation programs that target the cognitive deficits commonly observed after CABG surgery. The results reported here suggest that cognitive training could be involved as one component of a rehabilitation program. Future studies with larger cohorts of patients are needed to confirm this finding and to assess the relevance of using cognitive training as part of a broader and integrated rehabilitation strategy to enhance cognition and quality of life of older patients that underwent CABG surgery.

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