**A feasibility study of a group-based compensatory cognitive remediation therapy for individuals with subjective memory complaints**

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**Abstract (150-200 words)**

Cognitive remediation is a non-pharmacological treatment demonstrated to be effective to improve measures of memory, knowledge of memory strategies, mood, and psychological well-being in patients with mild cognitive impairments. The objectives of this feasibility study were to (1) explore whether or not the French version of SYNAPSE - a group-based compensatory cognitive remediation program developed in United States – could improve memory and other cognitive domains in individuals with subjective memory complaints (SMC); (2) evaluate the applicability and acceptability of the program in French-Canadian memory clinic care. Eight participants enrolled in the study and XX completed the program. Participants improved on measures of subjective and objective verbal memory as well as working memory and executive functioning. The program was demonstrated to be acceptable by the participants even if 37.5% of attrition was observed. Interestingly, those who dropped out had lower insight (i.e., fewer complaints and more verbal memory difficulties) than the completers. This preliminary study yielded clinically helpful data demonstrating the feasibility of the francophone version of SYNAPSE program in patients with SMC.

**Keywords**

Cognitive remediation, Subjective memory complaints, compensatory strategies

Word count:

**Introduction**

According to the new National Institute on Aging-Alzheimer’s Association / International Working Group research criteria, Alzheimer Disease (AD) can be subdivided in three stages: an aymptomatic or preclinical stage, a stage of Mild Cognitive Impairment (MCI), and the dementia stage (Dubois et al., 2010; Sperling et al., 2011; Visser, Vos, van Rossum, & Scheltens, 2012). In the last decade, the dementia stage of AD has generated a considerable amount of interest. Cognitive impairments, especially memory impairments, are a well-known marker of this stage. Then, the concept of MCI has emerged and quickly spread, as it described a new clinical entity: elderly patients with cognitive complaints and cognitive decline, objective impairment in memory and/or other cognitive domains, but no major repercussions in daily life, and are not demented (Petersen, 2004; Petersen et al., 1997; Portet et al., 2006). Nowadays, clinicians begin to focus on the asymptomatic / preclinical stage in order to prevent the risk of developing dementia. This stage was differently labeled in the literature: subjective cognitive impairment (e.g. Reisberg et al., 2008), subjective memory impairment (e.g. Jessen et al., 2010) or pre-MCI (e.g. Duara et al., 2011; Nunes et al., 2010). Currently, researchers agree to use the term Subjective Memory Complaints (SMC) as this terminology does not imply the presence of impairment, but a complaint (add references).

SMC may be qualified as a pre-clinical indicator of eventual cognitive decline, hence the term "pre-MCI" (Jessen et al., 2010). Indeed, longitudinal cohort studies (Jonker, Geerlings, & Schmand, 2000; Reid & MacLullich, 2006) among older subjects without cognitive impairments identified SMC could be a predictor of cognitive decline and dementia. Among subjects who are classified as pre-MCI, based only on informant reports, it has been reported that 90% have AD pathology at autopsy (Storandt, Grant, Miller, & Morris, 2006).

The label SMC has been used to describe subjects who are presumed to be in a very early stage of AD, when cognitive function is in the normal range, but an increased risk for progression to dementia is suggested either by subjective memory complaints, or biomarkers suggest the presence of the disease (e.g., regional brain atrophy) (Jonker et al., 2000; Wang et al., 2004). In other words, patients with SMC are patients with prominent cognitive complaints, but in whom neuropsychological tests do not show abnormal results (Nunes et al., 2010). This stage appears to last about 15 years before the presently well-recognized MCI cognition (Reisberg et al., 2008). Therefore, interventions such as cognitive remediation, might need to begin during this stage, as cognition is still intact, but at risk.

There is a high comorbidity between subjective cognitive complaints, progression to MCI/AD and depression (Steffens, Fisher, Langa, Potter, & Plassman, 2009). Indeed, a longitudinal study showed that 63.3% of patients with MCI had depressive symptoms (Solfrizzi et al., 2007) and late life depression is associated with increased risk of subsequently developing dementia (Barnes et al., 2012; Diniz, Butters, Albert, Dew, & Reynolds, 2013).

Within the last 20 years, several standardized cognitive trainings have been developed, aiming at delaying cognitive decline in older people who are at risk of AD or in mild stages of dementia. A number of recent randomized controlled studies with MCI participants have demonstrated that cognitive training can improve measures of memory, knowledge of memory strategies, mood, and psychological well-being (Belleville, 2008; Hampstead, Stringer, Stilla, Giddens, & Sathian, 2012; Huckans et al., 2013; Olchik, Farina, Steibel, Teixeira, & Yassuda, 2013; Teixeira et al., 2012). However, the transfer of cognitive training effects into activities of daily living was very limited in most previous studies (Kasper et al., 2015) and the duration of these effects are unknown. A recent review of literature (Kasper et al., 2015) showed that another approach of cognitive remediation, called *cognitive rehabilitation*, is effective to improve memory performance and competence of activity of daily living in mildly cognitively impaired subjects. This kind of approach attempts at integrating compensatory elements into the treatment plan and showed that greater effects of cognitive rehabilitation were observed if the intervention was offered in earlier stages of cognitive decline. Others have recommended that future research could concentrate specifically on training MCI patients how to use external aids to compensate for memory difficulties (O’Sullivan, Coen, O’Hora, & Shiel, 2015). These reports are congruent and support the idea that the implementation of a cognitive remediation program focusing on compensatory strategies and offer these at a pre-clinical stage (i.e. patients with SMC) would be more efficient.

Elderly people presenting with subjective cognitive complaints may be in an initial phase of a degenerative disorder and should be followed clinically, even if they have normal neuropsychological test performances. The construct of SMC identifies individuals earlier in the process of cognitive decline. Therefore, clinicians have the opportunity to intervene earlier in this process, perhaps preventing or delaying further cognitive decline (Albert et al., 2011). People with MCI have cognitive impairment but minimal impairment in complex instrumental activities and are functioning more or less independently. Therefore, Belleville (2008) suggested that cognitive intervention may benefit persons with MCI because they retain the cognitive capabilities to learn and apply sets of new strategies. This idea would definitively extend to people with SMC because they have no cognitive impairment, hence better capacity to process and retain verbal information in memory and are functioning independently. Cognitive remediation will also benefit to people with subjective memory complaints as they also have relatively intact cognition but are bothered by the subjective experience of memory difficulties.

There is growing interest in developing interventions for people with subjective memory complaints, in order to intervene at an earlier point on the trajectory of possible neurodegeneration and to exploit cognitive plasticity and foster independent functioning. To our knowledge, very few published studies have investigated cognitive rehabilitation in patients with SMC, whereas the effectiveness of interventions in AD population have been well-documented (Sitzer, Twamley, & Jeste, 2006) and promising for MCI population (Huckans et al., 2013). A meta-analysis of cognitive training in AD population (Sitzer et al., 2006) showed that compensatory strategies have to be used before the diagnosis of AD because the difficulties experienced by AD patients may present a unique challenge to teaching compensatory strategies as they may forget to use them. Moreover, studies showed that benefits of cognitive intervention are greater for patients in early stages of cognitive decline (Bahar-Fuchs, Clare, & Woods, 2013; Kasper et al., 2015). Therefore, one crucial method for preventing the incidence of AD and other dementias in society, and for helping older adults currently suffering from cognitive difficulties, would be to implement advanced clinical care practices in memory clinics that treat outpatients with SMC to help either remediate the cognitive deficits observed in these patients or prevent and/or delay their progression of their impairment to AD or other dementias. Motivationally-Enhanced Compensatory Cognitive Training (ME-CCT) for MCI seems to be the new appropriate intervention to use because it is highly feasible, low-cost and low-tech, can be easily incorporated into healthcare system and includes multi-modal techniques.

*Current study*

The objectives of this feasibility study were to (1) **translate** **and adapt** the Motivationally-Enhanced Compensatory Cognitive Training intervention for MCI for French-speaking patients with SMC; (2) use it **earlier** in the life course by offering it to patients with SMC without objective cognitive impairments. This means that the intervention is applied earlier allowing cognitive rehabilitation to act as a form of prevention for further cognitive decline; (3) **evaluate** the applicability and acceptability of the program in French-Canadian memory clinic care; (4) **explore** whether the French version of the cognitive remediation program - called SYNAPSE in French - improves memory (objective and subjective measures) and other cognitive domains in individuals with SMC.

The validated intervention was first implemented for clinical purposes, in its original English version. Clinicians delivering the sessions were trained by reading the intervention manual. A neuropsychologist (G.G.) met with other professionals (psychologist, occupational therapist, and recreational therapist) on 3 occasions (total of 9 hours) to explain the cognitive rationale behind the interventions, session by session. Comments and observations from the clinicians were collected at the end of each meetings to help adapt to the local population: (1) the visual aspect and quantity of written information in the manual was too heavy for participants to follow on their manual (complaints of both patients and clinicians); (2) patients looked tired at the end of the session; (3) some examples were inappropriate for this age group; (4) there was no simpler version for the participant to follow during sessions and (5) there were no instructions, recommendations or explanations for the clinicians.

**Method**

*Participants*

The aim of the present project was to investigate the applicability of a cognitive remediation program for outpatients with SMC. This research project was approved by the appropriate ethics committee at the Douglas Mental Health University Institute, Montreal, QC, Canada. Participants were informed that they could withdraw from the study at any time. Individuals for this study were recruited from outpatient pool of the Memory Clinic service of the Douglas Mental Health University Institute, which is a third line psychiatric service providing specialized care for clients aged 65 and older and younger adults with memory difficulties.

Inclusion criteria were: a) to present a subjective memory complaint but relatively normal scores on cognitive screeners (MMSE score≥24).

Exclusion criteria were: a) neurological disorders (traumatic brain injury, epilepsy), b) lifetime history of any non-mood psychotic disorder (e.g., schizophrenia); c) current substance or alcohol dependence (within the past 3 months); d) current diagnosis of delirium, dementia or other neurocognitive disorder; e) uncontrolled clinical disease (e.g., cardiovascular, renal, pulmonary); and f) unable to consent to be part of this research protocol.

People suffering from depression or anxiety were included for external validity of the research as there is such high comorbidity with subjective cognitive complaints. This ecological setting highlights the reality in gerontology, where comorbidity is the rule rather than the exception.

Ten participants were informed about the study and given the opportunity to participate. All accepted the invitation. For this first cohort, a total of eight participants were included, from the 10 initially recruited. One participant was excluded because he did not meet inclusion criteria (very low scores on cognitive screeners) and one cancelled her participation one week before the beginning because of lack of motivation. Descriptive data are presented in Table 1.

**Insert Table 1. Demographic and clinical characteristics for patients with MCI**

*Procedure*

Following enrollment, self-administered questionnaires were sent to the participants two weeks before the beginning of the intervention. They had to complete all the questionnaires and bring them the day of baseline testing. The administration of tests at baseline took approximately two hours and was performed by a neuropsychologist. One week after, participants with SMC underwent a 8-week cognitive remediation program called SYNAPSE. Within two weeks after the intervention, the same self-administered questionnaires were sent and a post-test was performed with the same neuropsychological tests.

*Outcome measures*

In the present study all interviews and ratings were carried out by a neuropsychologist with experience in clinical research.

1. Screening tests:

* The Mini-Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) was used to assess general cognitive function and screen for cognitive impairment, track cognitive change that occurs with time, and assess the effects of potential therapeutic agents on cognitive functioning. It assesses orientation to time and place, attention and calculation, language and immediate and delayed recall (Folstein et al., 1975).
* The Montreal Cognitive Assessment (MoCA) (Nasreddine, Phillips, Bedirian, et al., 2005) was used to assess general cognitive function and was speciﬁcally developed for the screening of milder forms of cognitive impairment. Thirty items could be categorized into the following cognitive domains: executive functions; visuospatial abilities; short-term memory; language; attention, concentration, and working memory; and orientation to time and space (Nasreddine, Phillips, Bedirian, et al., 2005).

2. Measures of mood and personality:Depression and anxiety are frequent comorbidities of subjective cognitive complaint; so it would be relevant to know if SYNAPSE impacts on these set of symptoms.

* The Geriatric Depression Scale (Yesavage et al., 1982) was used to assess affective and cognitive aspects of geriatric depression. The GDS is a 30-item self-report measure of depression that is answered in a simple yes or no format in reference to how patients felt over the past week.
* The State-Trait Anxiety Inventory (STAI) (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983)is a commonly used measure of trait and state anxiety. It can be used in clinical settings to diagnose anxiety and to distinguish it from depressive syndromes. STAI has 20 items for assessing trait anxiety and 20 for state anxiety on a 1-4 scale (almost never-almost always).

3. Objective measures of cognition

* Cogstate battery (Westerman, Darby, Maruff, & Collie, 2001) is a cognitive battery that can be administered on a computer under supervision of training staff. The administration of the battery is standardized. Data processing and scoring is automated and norms are provided. The battery comprises a number of individual tasks – each designed to test a specific area of cognition. The selected battery includes measures of psychomotor function (Detection task), visual attention (Identification task), visual learning and memory (One card learning task and Paired associate learning task), verbal learning and memory (International Shopping List), working memory (One Back task), executive function / spatial problem solving (Groton maze learning test).

4. Subjective measures of cognition

* The “Self-reported memory questionnaire” (*Questionnaire d’Auto-Evaluation de la Mémoire*-QAM in French) (Van der Linden, Wijns, Von Frenkell, Coyette, & Seron, 1989) is a memory self-rating scale from 1 (never) to 6 (always) that contains 64 questions divided into 10 sections representing different areas of the memory.
* The Cognitive Problems and Strategy Assessment (CPSA) (Twamley, Vella, Burton, Heaton, & Jeste, 2012) is a self-report questionnaire assessing cognitive problems and cognitive strategy use (scale from 0-never to 3-always).

5. Measures of client satisfaction and acceptability of the program

* The Client Satisfaction Questionnaire (CSQ-8) (Larsen, Attkisson, Hargreaves, & Nguyen, 1979) is an 8-item self-report questionnaire using a 4-point rating scale that addresses satisfaction with services. This questionnaire was only administered at post-test.
* The Acceptability Questionnaire (Gagnon & Masson, not published) was used to assess the achievement of the class goals, satisfaction of the client concerning the structure of SYNAPSE (group, duration, tools, group leader…) and recommendations to improve the program.

6. Measures of patients’ participation

* The Group work Engagement Measures (GEM) (Macgowan, 1997) assess a group member’s engagement. The measure is to be completed by the group facilitator for each participant. The answer should be based on a typical session (the current or last session).
* Homework compliance and attendance: as prescribed in the intervention manual, the facilitator reviews home exercises at the beginning of each session. This information is also recorded and added to data as ‘number of home exercises completed’. The number of sessions attended is also recorded. Finally, the accomplishment of 2 specific home exercises was also recorded as a measure of compliance and prospective memory (to call and leave a voicemail for the facilitator on a given Saturday on 2 specific occasions).

*Cognitive remediation intervention*

SYNAPSE is a cognitive remediation program using compensatory strategies. It was first developed and validated for psychotic patients and named Compensatory Cognitive Training (CCT) (Twamley et al., 2012) and later adapted for individuals with brain injuries (Storzbach et al., 2016; Twamley, Jak, Delis, Bondi, & Lohr, 2014; Twamley et al., 2015) and older adults with MCI (ME-CCT). It consists of an 8 sessions of cognitive remediation program with one 2 hour session per week. The themes approached are various as follows: lifestyle strategies, utilization of calendars, organization, prioritization, prospective memory (i.e. memory for future events), attention, working memory, learning and long-term memory, decision-making, problem-solving, planning, and skills integration. SYNAPSE is a highly feasible, low-cost, low-tech cognitive rehabilitation intervention that can be administered by most allied health professionals and can easily be incorporated into the menu of typical mental health or primary care classes offered by many healthcare systems. Nevertheless, the intervention is comprehensive (i.e., entails cognitive training, psychotherapeutic, and lifestyle techniques) and multi-modal (i.e., targets attention, memory and executive function skills). SYNAPSE incorporates compensatory cognitive training techniques designed to help patients manage problems with memory, attention, and executive functions (i.e., organization, planning, decision-making, and problem-solving/mental flexibility); mindfulness-based stress reduction practice, which has been shown to improve cognitive and neuropsychiatric function in various populations, and, brief motivational interviewing techniques to increase engagement in healthy lifestyle behaviors associated with reduced risk for cognitive decline, MCI and dementia (i.e., physical exercise, mental exercise). Participants are also encouraged to use an electronic or paper calendar system of their choosing. Participants receive extensive training in and practice with their calendars, with a particular focus on how the calendar can facilitate their use of other strategies taught in the group. Participants are given class manuals and weekly home exercises so they can practice and implement skills in their daily lives. Home exercises are discussed at subsequent sessions so that participants can receive feedback and troubleshoot application of new skills to their specific real life goals and problems. In order to reduce fatigue and improve concentration, a five to ten minute break is taken after the first hour of the group, and shorter two minute breaks are taken every twenty to thirty minutes. Significant others are invited to attend the last sessions of SYNAPSE during the review of the skills taught and how to reinforce them at home.

*Translation and adaptation of the intervention*

The first step of the project was to translate and adapt the ME-CCT manual to the French-speaking SMC population.

*Manual*. The main changes consisted of: (1) decreasing the content by 30-40%, simplifying the content and wording, deleting all scientific language, (2) reducing the level of cognitive load in learning materials, to allow patients to follow during the sessions (G. A. Miller, 1956), (3) adding pictures to serve as visual cues about ongoing activities (e.g., personal reflection, group exercise, things to keep in mind), (4) adding recommendations and clear instructions for the therapist on each session in the facilitator’s manual (increasing the number of pages to 359), (5) adapting the examples for our population with SMC and to Canadian culture, adding more real-life examples to support understanding and transferability of some strategies, (6) adding hand-on activities (like writing values on objects to bring home) and role plays, (7) streamlining the progression of topics, (8) adding a section at the end of each session to summarize the relevant information, (9) removing the section about MCI diagnosis because the patients included in the current study do not have such diagnosis, (10) adding new memory strategies efficacious for this specific population (Schacter, 1985), including spaced retrieval strategy (e.g. the method used in Baycrest, Toronto, Troyer, Murphy, Anderson, Moscovitch, & Craik, 2008); (11) changing formulation, pronouns, and verb tense to be less directive to foster motivation and limit possible invalidation (Cummings, Cooper, & Cassie, 2008; W. Miller & Rollnick, 2012) (e.g. take out all words like "good" and "bad", explain rationale rather than impose a solution); (12) adding information and empirical references to explain and support the concepts and strategies in the facilitator’s manual.

*Statistical analyses*

Statistical analyses were performed using SPSS, version 14.0. Due to the small sample size, non-parametric tests were used. The unpaired Mann-Whitney U-test was used to determine the differences between characteristics (e.g. age, education, depression, anxiety) of participants who completed the cognitive remediation program and the participants who dropped out.

For those who completed the program, a difference between baseline and post-test scores was calculated with the paired Wilcoxon test.

For all statistical analyses, effect size was reported in addition to traditional significance tests (*p*) to describe size of effect, independently from sample size (Sullivan & Feinn, 2012). Indeed, sample size of this feasibility study was small, and sometimes a statistically significant result only means a very large sample size was used (Ellis, 2009). Effect size was calculated with the following formula: Z score/√N. The resulting effect sizes may be interpreted as follows: changes of 0.2 - 0.4 are considered small, 0.5 – 0.7 considered medium, and ≥ 0.8 considered large (Cohen, 1988).

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**Results**

*Feasibility and acceptability*

Of the eight participants who began the cognitive remediation program SYNAPSE, five (62.5%) completed the program and three withdrew. From these three, one completed 7/8 sessions, another completed 2 sessions and the last one withdrew after the pre-test. The reasons for drop-out were: lack of motivation, excessive fatigability, and mismatch of service with expectations. Additionally, one participant who completed the program did not want to complete the post-test without giving specific reason except “I do not want”.

At the end of the CR program, patients (N = 4) were surveyed to gauge acceptability and satisfaction with the program. The results of the CSQ showed that they were generally satisfied by the program.

In the acceptability questionnaire (Gagnon & Masson), some questions were asked to help assessing whether they felt SYNAPSE could be delivered in this modality. Three participants on four answered that they were satisfied by all modalities of SYNAPSE, including group format, length of program (8 weeks), length of session (2 hours), frequent break, material and group leader. The other participant was satisfied by all modalities except the group format and the length of program (too long). This questionnaire also asks questions about the efficacy of the program to reach their goals and they all answered yes moderately.

*Adherence to the program*

Adherence was monitored weekly by the study staff. The five participants who completed the intervention and the sixth who finished 7/8 sessions were included in the analyses for adherence. The mean number of sessions attended for SYNAPSE was 7.33 ± 0.82.

In the acceptability questionnaire (Gagnon & Masson), some questions were about their motivation. Participants answered that their general motivation was moderate-high, their participation in class moderate and their motivation to do the homework moderate-low.

Finally, a questionnaire was filled by the group leader to measure the group work engagement (GEM). According to the group leader, participants who completed the program were often engaged in the group. Several variables were assessed and those with the highest scores are (Table 2): contracting (e.g. participants did not express any disapproval during the class), attending (e.g., arrive on time), and relating to group leader (e.g. follow the guidance, make contact). However, two variables generally showed lower scores: working on own problems and working with others’ problems. An interesting result is the fact that the general score of engagement of persons who dropped was lower (Mean = 2.23; SD = 0.63) that the score of persons who completed (Mean = 3.56; SD = 0.48) with a moderate effect size (ES = -0.73) (Table 2)

**Insert Table 2. Group engagement measure for patients who completed at post-test and comparison of the engagement between patients who completed and drop-outs at the beginning**

*Neuropsychological and clinical results at baseline*

Table 3 shows neuropsychological results of all patients at baseline. The screening tests showed that 3/8 participants have objective memory difficulties on the MoCA test whereas nobody had impairment with the MMSE test.

**Insert Table 3. Neuropsychological and clinical results of all patients at baseline (N=8) compared to the norm**

For *subjective memory complaints* (see QAM results), 2/8 participants have greater memory complaint than the general population. In our sample, thematic that people most complaints about were: conversation, slips of attention and places. More precisely, participants reported difficulty following a conversation because they forget what has just been said; difficulty in slips of attention resulting by forgetting where they have just drop off an object or enter a room to do something and forgot what it was that they wanted to do; and problems with places resulting by difficulty in learning a new itinerary or explaining to someone an itinerary or recognizing places that they are familiar with.

The *strategies* (see CPSA results) they mostly used in their daily life (mean answer ≥ 2 – corresponding to the answer “often”) before the beginning of the cognitive remediation program are the following: (1) use a calendar regularly to schedule and remember appointments and activities, (2) keep a written list of appointments, (3) remember where things are by putting them in the same place all the time, (4) If something have to be remembered, write it down somewhere, (5) make eye contact with someone who is talking to help understanding what is being said.

Concerning *objective measures of memory* (see Cogstate results), 4/8 participants had significant deficits to remember a shopping list at immediate recall and 3/8 at delayed recall (mean = 4.75 words; SD = 2.38), 2/8 in an identification task, 3/8 in a working memory task, 2/8 in an executive function task at immediate recall and 4/8 at delayed recall (Groton maze) and 1/8 in a visual learning task (Continuous paired association).

Concerning *clinical symptoms* (see GDS and STAI results), three participants had moderate depression and nobody suffered from anxiety.

*Changes between baseline and post-test*

Of the eight participants who began the cognitive remediation program SYNAPSE, five (62.5%) completed the program and three withdrew. Among the five who stayed, one did not want to pass the post-test assessment.

For those who completed post-test (N=4), neuropsychological and clinical results were compared with baseline results (cf. Table 4).

**Insert Table 4. Comparison of neuropsychological and clinical results between baseline and post-test for patients who completed**

Table 4 shows comparisons of neuropsychological and clinical results between baseline and post-test. Because of the small sample size, statistical test could fail to show significant difference even if it is exists (Sullivan & Feinn, 2012), therefore the emphasis was placed on effect size rather than statistical significance.

Concerning subjective memory complaints (see QAM results), there is moderate effect size (ES = -0.73) which shows that participants complaints less about memory after the cognitive remediation program (Mean = 2.61; SD = 0.57) than before (Mean = 3.12; SD = 0.95) in a general way. Indeed, their mean answer change from “sometimes” to “very rarely”. This is confirmed by the CPSA *memory complaints* (ES = -0.73).This decrease of memory complaints is observed in all QAM subscales with more or less magnitude. Two of them tended to be significant with fewer complaints after the CR program: movies and book, and political and social events. Moreover, a large effect size was observed for conversation and moderate effect sizes for slips of attention, people, use of objects, and actions to perform.

Concerning the strategies (see CPSA results), a moderate effect size (ES = -0.73) shows that participants use more strategies after SYNAPSE program than before.

Concerning objective measures of memory (see Cogstate results), participants improved in almost all cognitive processes regarding effect sizes. Moreover, concerning verbal memory (shop list immediate and delayed recall) two subscales tended to be significant with better scores in post-test compared to baseline with strong effect sizes. Results show moderate effect sizes for one-back task, one-card learning and Groton maze recall with a decrease of number of errors in post-test compared to baseline.

Concerning clinical symptoms (see GDS and STAI results), the cognitive remediation program did not impact significantly on these measures. However, anxiety-trait decrease in spot-test with a small effect size (ES =-0.27).

*What works for whom?: Comparison between participants who completed and those who dropped*

In order to better understand why some participants withdrew from the cognitive remediation program, a between-group analysis at baseline was done between the participants who completed the program (N=5) and those who dropped (N=3). A particular interest was given to effect sizes suggesting moderate and strong effect (0.5 and higher).

**Insert Table 5. Comparison of neuropsychological and clinical results at baseline between patients who completed and drop-outs**

Table 5 shows interesting group difference in participants’ characteristics, when it comes to subjective and objective memory measures. Participants who dropped were younger, had higher level of education and got better scores to the screening tests (MMSE and MoCA) with small effect sizes. Moreover, a moderate effect size (ES = -0.47) for QAM total mean indicates that participants who dropped had less memory complaints (Mean = 2.13; SD = 0.76) than those who completed (Mean = 3.03; SD = 0.76) and this is confirmed with the CPSA memory complaints (ES = -0.37). This pattern is actually found on all QAM subscales, with variable magnitude. However, regarding verbal memory performance (Cogstate - learning of a shopping list), a moderate effect size suggested that participants who dropped recalled less information (Mean = 16.33; SD = 1.53) than participants who completed (Mean = 20.00; SD = 4.18). In other words, those who dropped the program had fewer memory complaints but more objective memory difficulties. In addition, participants who dropped reported using more strategies than the others (ES = -0.26).

Finally, concerning the *clinical symptoms*, participants who completed the program tend to have (small effect size) higher scores on depression and anxiety measures.

**DISCUSSION**

The objectives of this feasibility study were to (1) evaluate the applicability and acceptability of the program in French-Canadian memory clinic care; (2) explore whether the French adapted version of SYNAPSE – a group-based compensatory cognitive remediation program developed in United States – could improve memory and other cognitive domains in individuals with SMC. The program was demonstrated to be acceptable even if 37.5% of attrition was observed. The preliminary results indicated that patients who completed (N=4) the program seemed to improve both subjective and objective verbal memory and also to improve in other cognitive domains such as working memory and executive functioning. Interestingly, the dropouts’ participants had lower insight (i.e. fewer complaints and more verbal memory difficulties) than the completers.

*SMC group compared to the norm*

The study group (N=8) had some specific characteristics compared to the persons of the same age in the general population (i.e. norm). The MMSE screening test showed no significant impairment whereas the MoCA showed that 3/8 participants were below cognitive impairment threshold, which is congruent with the literature showing that MoCA is more sensitive than MMSE (Nasreddine, Phillips, Bédirian, et al., 2005). This result suggests that some of them are at risk for MCI or dementia, as SMC has been identified as a risk factor for cognitive decline in older subjects (Jessen et al., 2010).

The neuropsychological results are congruent with people suffering from SMC as all of them had memory complaints identified by standardized questionnaire. However, when compared to the norms of the QAM, only two of them had significantly higher complaints than the general population of the same age. This highlights the difficulty to define this clinical population which could refer to individuals with SMC or individuals with more SMC than the average. The questionnaire provided some precisions about the kind of memory the current group specifically complained about: conversation, slips of attention and memory for places. The objective cognitive tests showed that indeed, verbal memory was significantly impaired (below the norms provided by Cogstate) for half of them, who had difficulties to recall a list of words immediately after the reading and at delay. Moreover, three of them had impairments in working memory (one-back task) and executive function (Groton maze learning task). However, visual learning seems to be preserved (Paired association and one card learning tasks), where the information only has to be held in visual memory for a short period of time (around 10 seconds to 2 minutes).

Results on questionnaire suggested the study group already used some compensatory strategies at baseline. However, detailed analyses showed only the basic ones such as the use of an agenda or note taking.

Finally, the group denied anxious symptoms but three of them reported moderate level of depressive symptoms. It is notable that depression can coexist in individuals with SMC. A study (Lautenschlager, Flicker, Vasikaran, Leedman, & Almeida, 2005) found that elderly (≥70 years of age) community-residing women with SMC had higher depression and anxiety scores than a comparison group of healthy community-residing women that was closely matched in terms of the level of cognitive scores. Accordingly, the comorbidity of SMC is high with anxiety and depression but this was observed only for depression in the current study.

*Improvement after the cognitive remediation program SYNAPSE*

Effect sizes indicated that ratings of general subjective memory functioning were higher after SYNAPSE cognitive remediation (ES = -0.73), and the magnitude of this improvement was even higher on objective verbal memory measures (ES = -0.92) in our small study group (N = 4). According to Floyd & Scogin (1997) who found the same comparison with larger effect size for objective memory measure, the main explanation for this difference is the fact that subjective memory evaluations are more resistant to change than is actual memory performance. However, given the frequency of memory complaints by people entering such remediation programs, effects on subjective aspects of memory are just as important as or even more important than objective memory performance change as indicator of success.

The participants complain less about their memory after the 8-weeks cognitive remediation program. This was observed in for a wide range of situations, with variable effect magnitude (from 0.18 to 0.82). At baseline the group complained a lot about conversation, slips of attention and memory for places; and at post-test they complaints significantly less about the two first and slightly less about the last one. This is congruent with the fact that SYNAPSE includes some specific strategies about memory during conversation (e.g. listen actively, eliminate distractions, ask questions and paraphrase) and attention (e.g. limit distraction, avoid multi-tasking) but very little about the memory for places.

On objective cognitive measures, verbal memory (immediate and delayed) which was impaired for half the group at baseline significantly improved after SYNAPSE. Moreover, large effect sizes were found on working memory (One-back task) and executive function (Groton maze recall). However, participants not improve in all cognitive processes at post-test; as visual attention, psychomotor function, and visual learning did not change between baseline and post-test. These results are in congruence with the specific topics discussed in the program, which focus on verbal memory, working memory and executive function (organization, solving-problem). In line with this, the only unexpected result would be the fact that visual attention did not improve while this cognitive process was targeted in SYNAPSE program, perhaps because this section is theory-based and no practice is done to apply the learning strategies. Contrastingly, strong improvement in verbal memory could reflect that participants applied the learning strategies during the post-testing. This hypothesis is supported by the fact that participants improved the general use of strategies after the cognitive remediation program (ES = -0.73). At baseline, they already use some basic strategies such as note taking and agenda; at post-test the strategies they mostly used are note taking and categorization. Therefore, participants may have used the categorization strategy during the verbal memory task helping them to remember the items of the shopping list.

The original English version of this compensatory cognitive program was used for patients with MCI. Preliminary results showed similar improvement in subjective cognitive functioning and use of strategies (ref). However, one difference between their study and the current one is the decrease in depression symptoms reported by MCI patients after the program whereas not in patients with SMC. Indeed, in the current study, no difference was found on depression scale between baseline and post-test which suggests that the decrease of memory complaints and the improvement of cognitive processes were probably attributable to the cognitive remediation program itself rather than to the secondary benefits of improved mood. Some studies provided support for the hypothesis that level of depression predicts level of cognitive functioning (Lichtenberg, Ross, Millis, & Manning, 1995). Therefore, it is important to partial out the combined effects of depression and age on cognitive functioning (Raskin, 1986). As literature showed that a decrease in depressive symptom is often linked with an improvement in cognitive processes (Geda, Knopman, Mrazek, & et al., 2006), it makes it difficult to disentangle the effect of the cognitive remediation program to the effect of changing mood. However, we can postulate that this specific cognitive remediation program allowed patients with MCI to improve both in cognitive and clinical symptoms because of the integration of lifestyle strategies and meditation which could have had an impact on mood. One explanation why patients with SMC did not decrease in depressive symptoms could be the fact that patients with MCI have much more symptoms of depression than patients with SMC (Yates, Clare, & Woods, 2013) and participants with worse scores at baseline are susceptible to improve more.

*Why some participants dropped – How avoid attrition?*

In the current study, there was 37.5% of attrition. Close analysis of participants who dropped outs can help better understand who is likely to stay vs drop out of this type of intervention. Therefore, individual’s characteristics were compared in order to identify potential predictors of treatment adherence.

First, participants who dropped out were younger, more educated and had better scores on screening tests (MoCA and MMSE). Hence, they may feel less concerned by this kind of intervention which is presented as rather “aged-oriented”. One recommendation for better adherence to the group could be that patients understand that the program do not target old people but people with memory complaints, which can occur at any age.

Second, participants who dropped had less memory complaints than those who completed (ES = -0.47). It could be explained by two main reasons: (1) because they commonly use more strategies; and/or (2) because they had lower insight. Indeed, the analysis revealed that dropouts reported using more strategies at baseline than the completers (ES = -0.26). Interestingly, the effect sizes highlighted that dropouts made more errors in working memory task and less items recalled in verbal memory (immediate) than participants who completed. Therefore, in the current study it seems that dropouts had lower insight, probably which would be deleterious to motivation and openness to try new strategies. This result indicates that subjective memory capacity beliefs were not only related to actual verbal memory performance in a group of patients with SMC. Lack of insight is a well-known, clinically challenging, phenomenon in patients with neurodegenerative diseases (Kalbe et al., 2005; Koltai, Welsh-Bohmer, & Schmechel, 2001). There is strong evidence that awareness of memory functioning can vary greatly among individuals with MCI (Roberts, Clare, & Woods, 2009). For example, one study would suggest insight in MCI, showing a relationship between subjective memory beliefs and objective cognitive performance only in people with MCI but no in group without impairment (Cook & Marsiske, 2006). Another study rather shows that unawareness of functional deficit predicted future progression to dementia (Tabert et al., 2002). According to the latter, the patients who drop-out in the current study have more probability to progress to MCI or dementia because they are unaware of their difficulties and as a consequence did not complete the program allowing them to improve.

Third, participants reporting more cognitive problems and less cognitive strategy use are the completers. This observation suggests that perhaps they had more openness to use new strategies or more motivation to address their cognitive problems (Twamley, Burton, & Vella, 2011).

Finally, participants who completed the program had slightly higher scores on depression and anxiety measures which could have motivated their presence to every session.

*Limitations and recommendations*

Several methodological limitations must be considered when interpreting the results of this feasibility study. First, the lack of control group does not allow conclusions about the *effectiveness* of therapy. Observed improvements may be attributable to non-specific effects rather than to cognitive remediation therapy *per se*. Second, the same neuropsychological tests were administered at baseline and at post-test. In the absence of a control group, it is impossible to rule out the possibility that neuropsychological improvements represent practice effects. Third, the small sample size greatly limits generalizations. Despite these limitations, this study yielded encouraging data that will inform the design of a randomized controlled trial which will permit to conclude concerning the effectiveness of the program.

Based on all observations made during this feasibility study, some changes have to been done for future administration of SYNAPSE: (1) to modify the 8 sessions into 10 sessions because the content is too important and pace too quick for patients with SMC, participants needed supplementary time, whereas it would be difficult to increase the duration of each 2-hours session, so we decided to change from 8 to 10 sessions, by keeping the same content but taking more time to explain, practice in class and correct the homework of the previous session; (2) to add some measure about participants’ readiness to change (e.g. URICA questionnaire); (3) to add a specific strategy for spatial memory as “memory of places” represented one of the most complaint of people with SMC at baseline and did not improve at post-test: the mental maps exercises have been chosen (Bohbot et al., 2012; Konishi & Bohbot, 2013); (4) to put more emphasis on visual attention as this cognitive process did not improve despite is already targeted by SYNAPSE: we chose to add some practical exercises in class (selective attention task, dual task, pay attention during the reading of a text, new play role…).

**Conclusion**

SYNAPSE cognitive remediation was demonstrated to be acceptable to participants with SMC as few of them withdrew, nearly all of them reported to be satisfied by all modalities of SYNAPSE, and SYNAPSE allow them to moderately reach their goals. The analysis of individual characteristics between dropouts and completers may highlight how to avoid attrition. Further randomized controlled studies of cognitive remediation in patients with SMC are now necessary to assess the effectiveness of SYNAPSE program.

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