

## THE EFFECT OF ATTENTION PROCESS TRAINING (APT-II) ON COGNITIVE AND DAILY LIFE FUNCTIONING IN PATIENTS WITH A MILD COGNITIVE IMPAIRMENT: A RANDOMIZED CONTROLLED TRIAL

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**Introduction.** Older adults with mild cognitive impairment (MCI) are at increased risk of developing dementia even if they do not meet the criteria for dementia. Executive control of working memory, which is implicated in divided attention, is often impaired in this population, and such impairment is a strong predictor of dementia. Slowing the development of dementia by enhancing cognitive and brain plasticity represents a current and future challenge for clinicians and researchers. Cognitive rehabilitation allows patients to compensate for cognitive deficits with the ultimate goal of reducing the impact of such deficits on everyday life. We aim to examine the effectiveness and generalization of an attention and working memory training program (Attention Process Training or APT-II) in improving cognitive and everyday functioning in patients with MCI by means of a single-blind, randomized controlled trial.

**Methods.** Twenty-Four MCI patients will be randomly assigned to either a "Cognitive Training with APT-II" group or a "Standard Care" group. Initially, patients will be administered a battery of standardized neuropsychological tests to ensure that they meet MCI criteria. The intervention will consist of a cognitive training program (APT-II) and will last 8 weeks (two sessions per week). One of the strengths of APT-II training is that it emphasizes the transfer of cognitive gains from training sessions to everyday life. To evaluate the treatment's effectiveness in improving cognitive and daily life functioning, cognitive and functional outcomes will be assessed just before, immediately after, 3 months after, and 6 months after the intervention program. A divided attention memory task performed in virtual reality will also be administered to evaluate the effects of APT-II training on the management of attentional resources in a relatively ecological situation.

**Perspective.** If our results indicate an improvement in the cognitive and daily life performance of older adults with MCI, this non-invasive, low-cost technique may deserve increased consideration as a therapeutic intervention to delay or reverse cognitive decline and diminish the risk of developing dementia in this population.

**Trial registration.** ClinicalTrials.gov, ID: NCT04606953, Registered on 28 October 2020.

**Keywords.** Working memory training (WMT), Mild cognitive impairment (MCI), Dementia, Cognitive rehabilitation, Attention

### Introduction

Seniors with mild cognitive impairment (MCI) have a cognitive complaint. The presence of one or more cognitive disorders is objectified by a patient's abnormal performance on standardized neuropsychological tests compared with their peers with respect to age and, if possible, education and gender<sup>(1, 2)</sup>. However, even if these individuals have an increased risk of developing dementia, they do not meet the criteria for dementia<sup>(1, 2)</sup>.

<sup>3)</sup>. In this way, MCI does not interfere detrimentally with everyday activities. Petersen<sup>(2)</sup> suggested a classification of MCI patients which includes a heterogeneity of cognitive profiles, with certain profiles indicating a higher risk of progression toward a specific dementia. Indeed, dementia is developed in 6-10% of people with MCI per year<sup>(4)</sup>, which is higher than the risk of dementia for the general population. This

incidence increases to 14.9% within 2 years for MCI patients over 65 years of age <sup>(4)</sup>. Nonetheless, it is important to note that not all people with MCI develop dementia; some MCI patients remain clinically and cognitively stable throughout their lives <sup>(5)</sup>. It has even been shown that some people with MCI regain cognitive abilities within the norm for their age <sup>(4)</sup>. In the current study, we aim to assess the efficacy of a cognitive training in mitigating the cognitive deficits associated with MCI and their subtle impact on daily life in MCI patients.

### **Neuropsychology of MCI:**

People with MCI may have a predominance of memory disorders (amnesic MCI, "a-MCI") or non-memory disorders (non-amnesic MCI, "na-MCI"). Amnesic MCI disorders are more common than non-amnesic MCI disorders <sup>(4)</sup>. In either case, a person with MCI may have a disorder of a particular cognitive function or an impairment of several cognitive functions, such as memory; attention; executive; language or visuo-spatial functioning. In addition to episodic memory deficits, the executive control is the most often impaired in MCI patients as indicated by their deficient performance in double-tasking situations <sup>(6)</sup>. Working memory (WM) disorders are also commonly found in both amnesic and non-amnesic elderly MCI patients. Such deficits are associated with a disturbance of the ability to manipulate information in WM, exercise inhibition processes, or manage double-tasking situations. It is important to highlight that these deficits in the ability to manipulate information in WM as well as attentional switching disorders have a high prognostic value for the development of Alzheimer's type dementia. Because of their WM deficits, elderly people with MCI are suitable candidates for WM training programs that aim to slow the deterioration of cognitive functioning and diminish the resulting subtle repercussions on daily activities. It is all the more relevant that WM is involved not only in many activities that require, for example, "reasoning, decision making, problem solving, learning and understanding of language" <sup>(7)</sup>, but also in the various complex cognitive and motor situations of everyday life <sup>(8)</sup>. Deficits in WM thus contribute significantly to other cognitive and functional impairments in MCI patients.

### **Contribution to the research:**

Some WM and attention training programs have been shown to induce an immediate positive impact on WM in older adults with MCI <sup>(6)</sup>. The aforementioned authors trained MCI patients with executive dysfunction to distribute their attention with variable priority between two tasks (six sessions of 1 hour each over the course of 2 weeks). Patients received feedback on their performance to help develop a self-regulation strategy. Patients receiving training with variable priority

between the two tasks significantly reduced the cost associated with the dual task compared with active controls. In addition, after these both programs, patients improved their performance on each of the two tasks administered in full attention as well as on tasks assessing selective attention, speed of processing, and alternating attention. Previous programs targeting WM processes have also been shown to induce positive gains in MCI patients. In 2013, Carretti and her collaborators <sup>(9)</sup> proposed a WM training for elderly patients with amnesic MCI (3 sessions of 30-40 minutes each over the course of 2 weeks). Patients involved in this training program experienced near transfer effects to visuo-spatial WM tasks and far transfer to a non-verbal reasoning task compared with an active control group (psychoeducation). Additionally, after WM training of elderly MCI patients with the Cogmed program (25 sessions, 2 sessions per week), improved performance on verbal and visuo-spatial WM tasks was also reported with long-term maintenance of these gains but no distant transfer to an episodic memory task <sup>(9)</sup>. Hyer *et al.* <sup>(10)</sup> also used the Cogmed program for training WM in patients with MCI. In their randomized controlled trial, 68 elderly patients with MCI were distributed between a group following a Cogmed training program with exercises of progressive difficulty (25 sessions of 45 minutes each over the course of 5 weeks) and another group involved in an identical computerized program with exercises that did not increase in difficulty <sup>(10)</sup>. For both groups, an improvement in WM was demonstrated after each training program. In addition, patients who completed the Cogmed program with exercises of increasing difficulty improved their performance on a visuo-spatial WM test and reported less difficulty in a functional activity questionnaire over the long term compared with patients whose exercises did not increase in difficulty. According to the authors, increasing the difficulty of the exercises increases the possibility of daily life transfers, although the precise mechanism for this remains to be described.

To date, the long-term maintenance of gains from WM training and the impact of such training on daily life have rarely been investigated in MCI patients. However, the functional state of the WM can predict the level of participation in daily living activities among the elderly <sup>(11)</sup>. The application of cognitive skills to ecological situations is all the more essential in elderly people with MCI as it can contribute to the maintenance of functional autonomy and quality of life. Few studies have focused on this topic. Findings are still limited in this population because the majority of WM training programs do not provide explicit instructions for generalizing the strategies acquired during training sessions to daily life activities. These programs often contain mainly computerized exercises and typically

lack home-based exercises<sup>(9, 10)</sup>. We propose to fill this gap using the Attention Process Training (APT-II) program, which focuses on the transfer of cognitive gains to daily life activities from the very beginning of its sessions<sup>(12, 13)</sup>. The English version has already been validated in populations presenting with cognitive impairments resulting from a number of neurological aetiologies<sup>(12, 13)</sup>, such as stroke<sup>(14)</sup> and small vessel brain disease<sup>(15)</sup>. In patients with stroke in the acute stage, immediate attentional gains that were maintained in the long term were reported following APT-II compared with a group of patients receiving the usual care<sup>(14)</sup>. In 2017, Pantoni *et al.*<sup>(15)</sup> reported the effectiveness of the APT-II program in patients with vascular MCI (small vessels brain disease), as evidenced by improved performance on sustained attention and episodic memory tasks after the APT-II intervention compared with patients receiving standard care. However, the efficacy of APT-II has never been studied in elderly adults with MCI. Even in the presence of encouraging evidence supporting the effectiveness of cognitive interventions in reducing cognitive impairment in this population, randomized controlled trials are needed to better understand the impact of this behavioral approach. Our main objective is to evaluate the short- and long-term effectiveness of a WM and attention training program (APT-II) on cognitive function and ecological activities in patients with MCI by means of a single-blind, randomized controlled trial. Our study originally will also assess daily life functioning using questionnaires and a virtual reality memory task performed under divided attention. The latter is a new technology that provides an ecological and objective measure for the evaluation of memory and other cognitive functions while simulating a naturalistic yet controlled environment<sup>(16)</sup>.

Our research presents several hypotheses:

- The primary outcomes of attention and WM are expected to improve in treated compared with non-treated patients. After the cognitive training program, MCI patients should demonstrate improved functional and well-being compared with the control patients receiving the standard cares.
- To assess remote cognitive transfer, we will also study the impact of the training on episodic memory.
- The APT-II program contains generalization exercises applicable to daily life that aim to improve the participant's overall quality of life. We aim to show a possible cognitive benefit on daily life

through a decrease in cognitive complaints and an increase in global well-being.

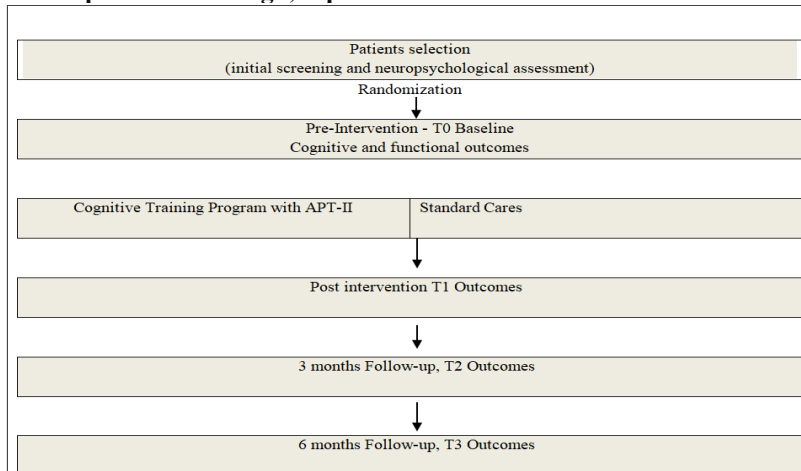
- Finally, we hope to observe the long-term maintenance of these cognitive and psycho-emotional effects by comparing the performances of patients who completed the APT-II program with that of the control group at a 6-month follow-up.

## Methods

**Study description, design and Ethics approval:** This study is a randomized controlled and single-blinded clinical trial. The design is illustrated in Table. 1. This study is registered at <https://clinicaltrials.gov> under the following registration number: NCT04606953. The study was approved by the Committee for the Protection of Persons Paris EST-III (BCR ID: 2018-A02377-48, CPP number: 18.11.05, n°18.08.21.66617). The patients will be informed both orally and in writing of the objectives of the study, their rights, and the progress of the project by either the principal investigators (MS) or one of the collaborating doctors (PM, EB). Each participant will receive a certificate of consent to verify their voluntary participation and consent. Participants will also be informed of their right to withdraw from the project at any time without penalty as well as their agreement to the use of the data collected. The signed consent forms will be kept by the principal researchers in a locked cabinet. For ethical reasons, the cognitive program will be offered at the end of the study to all participants who will want it but did not receive it.

## Randomization:

The protocol will be proposed to elderly people with MCI. After participating in the initial screening, gaining an understanding of the protocol, and submitting signed consent forms, participants identified as eligible will be enrolled in the protocol and randomly assigned to a “cognitive training” experimental group or a “standard care” control group. The randomization will be conducted per cluster and will be designed by group of four persons. A research assistant not otherwise associated with data collection will randomly assign participants into one of two groups using blocked randomization procedures. (Table 1). The experimental group will be participated in an 8-week intervention (2 sessions per week). All intervention sessions will be carried out individually at intervention sites or in the participant's home. Cognitive and daily life functioning will be evaluated using standardized outcome measures pre- and immediately post-intervention and at 3- and 6-months follow-ups after the end of the intervention. Assessors will be blinded to group allocation.

**Table 1: Experimental design, representation of the assessment and intervention****Participants and eligibility criteria:**

Twenty-four older adults with MCI will be recruited at various geriatric and neurological sites with the assistance of collaborating doctors from Tenon Hospital and Dupuytren Hospital (Public Assistance of Paris Hospitals), and the aid of private neurology clinics. Patients will be eligible if they meet MCI criteria according to Petersen <sup>(1)</sup>. Diagnoses will be determined using a multidisciplinary approach, including medical examinations, analyses of medical history, neuropsychological assessments, and/or brain imaging.

Patients should satisfy the inclusion and exclusion criteria (Table 2). All participants will receive a standard neuropsychological assessment, which will allow us to document the cognitive profile of the patients, determine the type of MCI, and thus confirm the study selection criteria. This first contact will also allow us to explain the research to the participants, fill out the health form, and provide a certificate of uncontented. The tests proposed for the neuropsychological assessment are presented in Table 2.

**Table 2: Inclusion and exclusion criteria**

<b>Inclusion criteria</b>	<ul style="list-style-type: none"> <li>- Being 55 years or over</li> <li>- Having normal or corrected vision and hearing</li> <li>- Being French speaker or bilingual</li> <li>- An impairment of episodic memory, attention and/or working memory evidenced by abnormal performance on neuropsychological test(s) evaluating these processes (-1.5 standard deviation under the norms for age and educational level)</li> <li>- Cognitive impairment without a significant impact on activities of daily living requiring external assistance or institutionalization</li> </ul>
<b>Exclusion criteria</b>	<ul style="list-style-type: none"> <li>- Dementia</li> <li>- Stroke, tumor, head trauma</li> <li>- Ethylism</li> <li>- Moderate to severe psychiatric disorders</li> <li>- Patients with severe depression (cut off &gt; 10 at the GDS 30 scale)</li> <li>- Patients taking treatments impacting cognition</li> <li>- General anesthesia in the last 6 months</li> </ul>

**Table 3: Neuropsychological standardized tests administrated during the initial neuropsychological assessment according to the different cognitive functions assessed**

<b>Episodic memory:</b> Auditory-verbal modality Visual modality	RL-RI-16 <sup>(17)</sup> <i>Rey–Osterrieth Complex Figure: immediate recall</i> <sup>(18)</sup>
<b>Executive functions and working memory:</b> Executive control Mental flexibility Speed processing Inhibition process	Letter-Digit Sequences (WAIS IV; <sup>(19)</sup> ) Code (WAIS IV; <sup>(19)</sup> ) Trail Making Test A & B <sup>(20)</sup> Stroop Color-Word Test-Victoria version <sup>(21)</sup>
<b>Language:</b> Lexical fluency	Verbal fluency (phonemic and semantic; <sup>(22)</sup> ) Denomination test (DO40, BECS-GRECO Version; <sup>(23)</sup> )
<b>Praxia:</b>	<i>Rey–Osterrieth Complex Figure: copy</i> <sup>(18)</sup>
<b>Mood assessment and questionnaire:</b>	Geriatric Depression Scale (GDS-30; <sup>(24)</sup> ) Lawton's Instrumental Activities of Daily Living Scale (IADL; <sup>(25)</sup> )

### Arms and interventions:

#### Working memory training:

The cognitive training program we will use is the APT-II <sup>(12)</sup>, which aims to train attentional processes and executive control of WM. This tool has been translated from English to French by S. Blanchet <sup>(13)</sup>, <https://www.lapublishing.com/attention-process-training-apt>). The program includes exercises that repetitively train different attentional components and the executive control system. These exercises of increasing and adaptable difficulty take place in both auditory and visual modalities. More specifically APT-II is used as intensive area-specific cognitive training. The program provides a theoretically based, individualized, and highly structured intervention of organized assignments at four attentional levels: sustained, selective, divided, and alternating attention. The first sessions will target selective and sustained attention; the following sessions, alternating attention; and the last six sessions, divided attention. Each session will last 1 hour and will be composed of three exercises with several items. The difficulty of the exercises will be adaptable according to the subject's performance, thus allowing them to improve over the course of the sessions while avoiding failure. The intensity of training, continuous feedback promoting motivation, and metacognitive training are factors that reinforce the benefits of the program. The experimenter will provide the participants with feedback about their performance after each exercise. Other aspects of performance such as patterns of errors will also be discussed. Our program has been designed to provide 16 sessions (2 sessions per week for 8 weeks). Training of such duration and intensity has already led to improved performance on attention and WM tasks as well as daily activities in a

pilot study of five elderly people with MCI <sup>(26)</sup>. The APT-II cognitive intervention will take place at one of the recruitment sites and/or in the homes of participants.

A unique feature of this program is its emphasis on the transfer of cognitive gains from the sessions to daily activities. To this end, patients will be invited to perform ecological exercises in autonomy between the different sessions. A logbook will be provided to each patient for the follow-up of these exercises. Such exercises enable the transfer of treatment tasks and techniques to self-selected cognitive problems in everyday situations.

#### Training of experimenters in administering APT-II:

The APT-II program will be administered by experts in neuropsychology (i.e., MS, a clinical neuropsychologist at the Public Assistance of Paris Hospitals) as well as neuropsychology students working towards their master's degrees in clinical psychology, who will assist the principal investigator (MS) in performing the program on patients. Both the aforementioned trainer (MS) and her supervisor (SB) will train students during the 3 years of data collection. The follow-up test examiner will receive individual training for each neuropsychological test to be performed to assure reliability and compliance to data collection procedures/standards and will perform the tests under blind conditions.

#### Control group condition – waiting list:

The control group will receive standard care, excluding speech and cognitive therapy. As with the experimental group, the control group will be assessed for cognitive and functional outcomes. At the end of the study period, the cognitive training program will be offered to participants who will not receive it (i.e., the control group).

**Outcomes measures:****Cognitive outcomes:**

An external neuropsychologist (ES) will evaluate the cognitive and functional outcomes under single-blind conditions. She will not be aware of the group assignment for each patient. Measurements will take place at baseline (T0), after the last training session (T1), and at 3-month (T2) and at 6-month follow-ups (T3). The follow-up measures at 3 and 6 months will be used to examine the long-term maintenance of the effects of the APT-II program. Alternative test versions or forms will be used when possible to avoid learning effects due

to repeated tests. The choice of standardized neuropsychological tests used as cognitive outcomes is based on an extensive search of studies using the APT-II tool with other populations, in which some tests have already shown sensitivity to the APT-II program.

**Primary cognitive outcomes:**

The primary outcomes, illustrated in Table 4, concern WM as measured by the Forward and Backward Digit Span <sup>(19)</sup>, the Brown-Peterson paradigm (Memoria version, <sup>(27)</sup>), the Paced Auditory Serial Addition Test (modified version <sup>(28)</sup>) and the Conners Continuous Performance Test 3rd Edition™ (Conners CPT 3™ ; <sup>(29)</sup>).

**Table 4: Primary cognitive outcomes**

<b>Tests.</b>	
Forward and Backward Digit Span <sup>(19)</sup>	The Forward Digit Span task assesses the phonological loop, whereas the Backward Digit Span task evaluates executive control of WM. This test consists of listening to a series of numbers read by the examiner. After each series, the patient must repeat the numbers in the same order (forward) or in the reverse order (backward). As the tests progress, the length of the lists is lengthened to increase the difficulty. After two failures in the same list length, the task stops. We will use two parallel versions (WAIS-III, MEM-III) counterbalanced between T0, T1, T2, and T3.
The Brown-Peterson paradigm <sup>(22)</sup>	The Brown-Peterson paradigm is an experimental technique used to study forgetting in short-term memory and also as a measure of the central administrator of WM. Subjects are presented with sequences of three consonants. After the presentation of each sequences, the subject is asked to either recall the consonants immediately or to count down from 30 seconds, 20 seconds, or 10 seconds. At the end of this interfering counting task, the subject is asked to recall the previous series of three consonants. We will use four parallel versions (MEMORIA version, <sup>(22)</sup> ) according to the counterbalancing table.
Paced Auditory Serial Addition Test (PASAT-4) <sup>(28)</sup>	The PASAT-4 evaluates information processing skills, sustained attention, and shared attention. The subject hears 61 successive numbers with an interval of 4 seconds between each number. The patient must add the first number in the sequence with the last one and give their answer out loud before the next item appears. This task requires the subject to perform a succession of simple addition calculations and solicit updating processes. The PASAT-4 test has already shown sensitivity to the APT-II program in a previous study on patients with a traumatic brain injury <sup>(14)</sup> and in a preliminary study in a population with MCI <sup>(26)</sup> .
Conners Continuous Performance Test (CPT) (Conners CPT 3™; <sup>(29)</sup> )	The CPT is a computerized task which evaluates sustained and selective attention <sup>(29)</sup> . This task consists of pressing the space bar on a computer keyboard after any letter is presented on the screen, except for the letter "X". This test lasts about 14 minutes.

**Secondary cognitive and functional outcomes**

Any changes in cognitive functions between T0, T1, T2, and T3 will be measured using the Mini-Mental State

Examination, (Greco version, <sup>(30)</sup>), Bravo's Scale <sup>(31)</sup>, the Cognitive Failure Questionnaire <sup>(32)</sup>, the Attention Questionnaire <sup>(12)</sup>, and a virtual reality task (see Table 5).

**Table 5: Secondary outcomes**

Tests.	
Mini Mental State Examination (MMSE) <sup>(30)</sup>	The MMSE is an assessment of overall cognitive efficiency. It is a cognitive debriefing scale that gives an overall score in the cognitive sphere and is widely used in clinical settings because it is brief. This test is intended as a means of diagnostic orientation when considering a diagnosis of dementia or other cognitive disorders. However, executive functions are not measured using this tool. Scores may range from 0 to 30 with a threshold pathological of 24-26 depending on the educational level.
Bravo's Scale <sup>(31)</sup>	This questionnaire is a measure of general well-being. It contains 18 items. The first 14 questions are answered on a 6-point Likert scale (0-5); the last four questions, on a 10-point scale (0-10). This gives a maximum score of 110.
The Cognitive Failure Questionnaire (CFQ) <sup>(32)</sup>	This self-reported questionnaire consists of 25 questions and aims to identify the consequences of cognitive problems on daily living <sup>(32)</sup> . Items are scored from 0-4, with a maximum total score of 100. High scores imply frequent cognitive problems.
The Attention Questionnaire <sup>(13)</sup>	This questionnaire concerns attention complaints reported by patients in their everyday lives. This questionnaire is included in the APT-II program.
Virtual reality task <sup>(33)</sup>	Episodic memory will be evaluated in an ecological situation by means of a virtual reality task performed under divided attention. This close-to-reality approach provides a deeper view of a person's functioning in daily life. The task assesses the components of episodic memory (factual, spatial, temporal, and perceptual details) using different recall modes (free and cued recall). The virtual environment consists of a virtual city displayed on a computer screen. Participants must "walk" in the streets of this city, following a marked path using a joystick <sup>(33)</sup> . Participants must first complete a familiarization task, in which they will have to memorize places (e.g. a town hall) along the way. At the end of this task, an immediate free recall test will be performed. This familiarization task will allow participants to grow accustomed to the virtual environment and the use of the joystick. Afterwards, 12 events (e.g., a woman fall because of a lamp post; see the appendix for all events) will be presented to the participant as they progress through the virtual city, and the participant will be instructed to memorize these events. At the same time, 40 sounds will be heard along the way, and participants will be asked to categorize these sounds as living (e.g., a dog barking) or a non-living sound (e.g., a horn honking) in real time. At the end of this encoding phase, subjects will complete the Brown-Peterson paradigm. After this interfering task, participants will perform a free recall of all remembered events as well as contextual information. This free recall session is followed by a cued recall session. The experimenter shows images of each of the 12 events one by one to participants, who are invited to recall as much information as they can related to these events, including spatial and temporal details. Finally, participants will perform delayed free recall of the living and non-living sounds that they previously heard during encoding, followed by an identification of these sounds.

### Data management:

Data will be collected anonymously after receiving the research participant's agreement. The anonymity of patients will be ensured by coding to respect confidentiality. Investigators will respect professional secrecy (according to the conditions defined by articles 226-13 and 226-14 of the Penal Code) and an ethical research agreement. Technical specifications of the trial database, such as the variables name, age, and disease diagnosis, will be predefined and documented in the patient database.

The original documents will be kept under lock and key by the main investigators of the study at Tenon Hospital in Paris. Personal information will be deleted 15 years from the end of the study. The results of the final analyses will be presented at scientific conferences and published in scientific journals.

### Statistics

To estimate the effect size of the sample for this clinical study, a power analysis was performed based on the results of our preliminary study <sup>(26)</sup>. In this previous study, 5 participants with MCI followed a cognitive training identical to the one described here but with a shorter duration (5 weeks, 2 sessions per week). We identified large effect sizes for performance on the Backward Digit Span test after the APT-II program. The mean score of the group at T0 (before the program) was 3.4 (SD = 0.54), which increased to 4.4 (SD = 1.14) after the training program. An a priori power analysis using G\*Power 3.1 software <sup>(34)</sup> indicated that, in order to obtain 80% power, a minimum of 22 participants (n = 11 per group) is required to detect a moderate to large effect size of 0.80 at the  $p < 0.05$  significance level.

Outcomes and questionnaires scores will be compared between the training group and the control group. Statistical analysis will be applied to all primary and secondary outcome measures in a comparative analysis of data collected at baseline (T0), after the last training session (T1), and at the 3- and 6-month follow-ups (T2, T3). We expect a larger improvement in the scores for the treated patients compared with patients in the control group. To study long-term effects, we will use an ANOVA model with the follow-up measurements. All tests will be two-sided at a 0.05 significance level. All statistical analyses will be carried out using R statistical software version 3.3.2 (R Foundation for Statistical Computing, Vienna, Austria).

### Perspective

By examining a possible method of enhancing the neurocognitive plasticity of elderly people at risk of dementia, this project may contribute to the research

issue of delaying the onset of dementia. It will also provide a new standardized rehabilitation tool for MCI patients in clinical practice, thus providing better care for these patients. The project could therefore have a major clinical impact.

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