

**Original Article**

# The Role of a Computerized Cognitive Intervention Program on the Neuropsychiatric Symptoms in Mild Cognitive Impairment

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## ABSTRACT

**Background/Purpose:** The effectiveness of therapeutic strategies is the subject of significant research in the field of Mild Cognitive Impairment (MCI). Computerized cognitive training is an example of a cognitive therapeutic intervention. As a risk factor for the development of dementia, the role of neuropsychiatric symptoms in the development of MCI is a significant field of study. According to earlier research, cognitive training can help with behavioral symptoms, and computerized cognitive education is thought to be a particularly successful method for treating neuropsychiatric dysfunction. The aim of the present study was to evaluate the outcomes of a personalized cognitive training program on the neuropsychiatric symptoms in individuals with MCI.

**Methods:** The sample consisted of 100 older adults with MCI, divided into two groups; with and without cognitive intervention, using the online Memory Motivation (MEMO) for six-months. All participants were assessed at baseline and after the completion of the training program with inventories that assess mood and anxiety.

**Results:** The results showed that the GDS ( $p < 0.001$ ), NPI ( $p = 0.043$ ), and HAMILTON ( $p < 0.001$ ) tests performed under the experimental condition had significantly lower results than those performed under the control condition.

**Conclusion:** The results of the application of the individualized cognitive training program showed a statically significant reduction in the neuropsychiatric symptoms in the experimental group. This result is consistent with earlier research that highlighted the benefit of cognitive training in reducing cognitive and behavioral symptoms, with long-term benefits in memory and depression. The study offers pertinent details regarding the implementation of a tailored intervention, the required amount of training time, and motivation as a key factor in the success of computerized cognitive training. Multidimensional cognitive education has been identified as a crucial strategy for preventing dementia and promoting healthy cognitive aging in the literature of suggested non-pharmacological interventions. The findings may be applied in clinical practice to develop strategies for preventing neurocognitive problems in the future.

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## 1. INTRODUCTION

The detection of underlying mechanisms and processes during the transition from cognitive healthy aging to the onset of dementia is of great interest. Various definitions have attempted to describe these changes, such as "senescent memory decline"<sup>1</sup>, "age-associated memory decline"<sup>2,3</sup>, "cognitively impaired not demented"<sup>4</sup> and "Mild Cognitive Impairment" (MCI)<sup>5</sup>, which depicts a transitional stage between healthy cognitive aging and the development of dementia. The most recent classification has been cited in the DSM-V<sup>6</sup>, "mild neurocognitive disorders".

In the area of cognitive aging, studies are now focusing on prevention in "asymptomatic" individuals at risk based on family history or genetic or neuroimaging evidence suggesting the onset of a neurodegeneration.

There is an intense research activity in the field of MCI regarding the effectiveness of therapeutic interventions. One such intervention is computerized cognitive training, a digital form of cognitive therapeutic intervention, where individuals can access different types of engaging activities and exercises from their own computers. In the study of Li et al.<sup>7</sup> the researchers concluded that there is no effective drug intervention in people with MCI with long-term benefits. They conducted a meta-analysis of seventeen clinical cognitive intervention studies for MCI. The results showed that after cognitive training, people with MCI improved significantly, both in overall cognitive functionality and overall self-assessment. The literature has focused more on the impact of interventions on cognitive skills.<sup>8-11</sup> Behavioral symptoms, such as apathy and depression, are common in people with neurocognitive disorders and contribute to the burden of caregivers and the quality of life of individuals.<sup>12</sup> The interest is focused on the search for non-pharmacological treatments for this category of symptoms, proposing interventions through new technologies and electronic software.<sup>13-16</sup> Possible advantages of using technology-based interventions include increased accessibility, reduced costs, the provision of rich experiences, and the adaptation of tests to individual performance. Researchers trying to explain the superiority of these interventions over the more traditional cognitive rehabilitation programs are considered to be related to usability and motivation, due to the interaction and real-time feedback from the technological medium, offering many promising beneficial effects.<sup>17-19</sup>

An important field of research is the role of neuropsychiatric symptoms in the development of the diagnostic category of MCI, being at the same time a risk factor for the onset of dementia. More specifically, the existence of depressive symptoms is such a risk factor.<sup>20</sup> The hypotheses are three, without being

mutually exclusive<sup>20</sup>: a) depression is a risk factor for cognitive decline<sup>21-23</sup>, b) cognitive decline is a risk factor for depression<sup>24</sup> Richard et al., 2013, c) and/or the existence of a third variable (neurological condition), which may simultaneously cause cognitive decline and depression.<sup>20,22,25</sup>

Depression, as a symptom, may not always be causative, but may exacerbate pre-existing cognitive decline by depleting cognitive reserve.<sup>25</sup> If depression is successfully treated, then MCI improves, but the person may be at greater risk of developing Alzheimer's disease.<sup>26</sup> Cognitive decline is considered as a symptom in elderly depressed patients. Pseudodementia is a syndrome that mimics dementia. However, the underlying cause is a psychiatric disorder which is usually, but not always, depression.<sup>20</sup> Understanding the etiology of neuropsychiatric symptoms in EGD may be important for understanding the development of dementia.<sup>27</sup>

The aim of the present study was to investigate the effect of an individualized cognitive training program on the neuropsychiatric symptoms of people with MCI.

## 2. METHODS

### 2.1. Participants

Data were analyzed from 100 participants, who met the diagnostic criteria for the diagnosis of MCI<sup>5</sup> and were under constant monitoring by the interdisciplinary team of the Outpatient Dementia Clinic of the University Neurological Clinic of the University General Hospital of Alexandroupolis, Greece. The final sample was divided into two groups depending on whether the participants attended the cognitive intervention program (target group) or continued their regular follow-up at the Dementia Clinic without receiving cognitive intervention (control group). Participants of both groups continued their regular clinic treatment. The randomized allocation was made by a third researcher blind to study groups. All participants signed a consent form before joining the study. The approval of the study was given by the Scientific Council of the University General Hospital of Alexandroupolis.

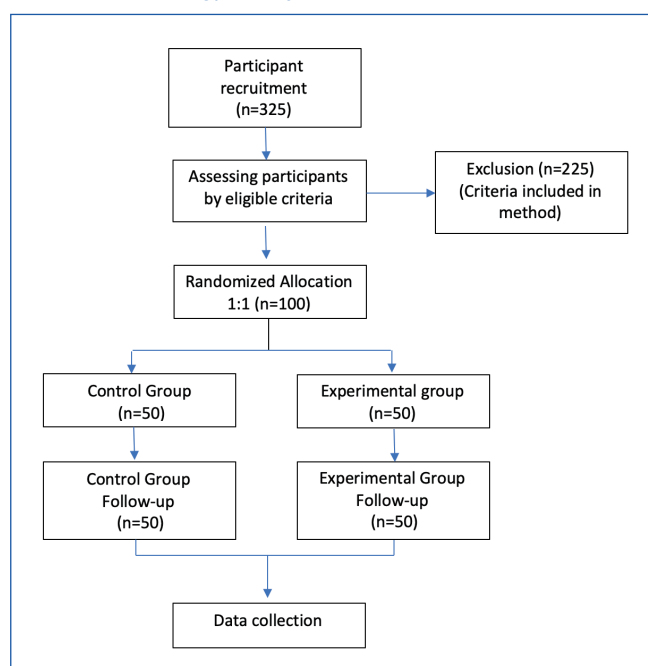
### 2.2. Inclusion/Exclusion Criteria

325 individuals underwent the interview (Figure 1), which consisted of biographical information and medical data, including information about any medical diagnosis, history of cardiovascular, metabolic and neurological syndromes and a history of potential affective disorders. Then they all underwent a neurological examination, a neuropsychological evaluation, a brain imaging, a biochemical and hematological examination.

A total of 100 individuals (Table 1) met the diagnostic criteria for the diagnosis of MCI, as codified in the

DSM-V<sup>6</sup>: a) subjective report of cognitive impairment, including reports from patient, family member or other informant or clinician; b) cognitive impairment for age, as evidenced by a formal neuropsychological examination; c) gradual reduction of objective cognitive skills - greater than expected for age - without falling within the range of diagnosis of dementia; d) maintained general cognitive and daily functioning; e) absence of previous diagnosis of dementia and other mental condition (e.g. depression, delirium, intoxication or psychosis), which could explain the observed impairment with a score on the Geriatric Depression Scale (GDS) <6.

**Figure 1. Methodology of subjects' recruitment**



**Table 1. Subjects' characteristics per group (n=100 subjects).**

	Control group	Experimental group
<b>Sex</b>		
Men	(16) 32.0%	(11) 22.0%
Women	(34) 68.0%	(39) 78.0%
Total	(50) 100.0%	(50) 100.0%
<b>Education level</b>		
≤6 years	(28) 56.0%	(21) 42.0%
7 up to 12 years	(5) 10.0%	(12) 24.0%
≥13 years	(17) 34.0%	(17) 34.0%
Total	(50) 100.0%	(50) 100.0%
<b>Age</b>		
≤65 years	(14) 28.0%	(9) 18.0%
66 up to 74 years	(21) 42.0%	(26) 52.0%
≥75 years	(15) 30.0%	(15) 30.0%
Total	(50) 100.0%	(50) 100.0%
<b>Diagnosis duration</b>		
≤2 years	(46) 92.0%	(37) 74.0%
≥3 years	(4) 8.0%	(13) 26.0%
Total	(50) 100.0%	(50) 100.0%

Exclusion criteria were the refusal to participate in the study, the presence of severe affective and mental disorders, certified by a score of 13 and above on the Hamilton depression scale, while anxiety disorders and depression are typically associated with debilitated cognitive functions.<sup>28-32</sup>

Other exclusion criteria were the presence of another serious systemic disease, the presence of severe visual and auditory deficits, which could interfere the performance of psychometric tests, secondary dementia and the systematic use of drugs with a direct effect on the CNS, such as benzodiazepines and neuroleptics. Patients with vascular risk factors were also excluded, as it is considered that vascular factors independently affect the development of cognitive functions.

### 2.3. Clinical Evaluation

The follow-up at the Outpatient Dementia Clinic was conducted by an interdisciplinary team that includes medical, nursing and other scientific staff. Data were recorded in an electronic individual form, which included social and demographic data, possible diagnosis, clinical examination findings, vascular risk factors, information on the onset and course of the disease, laboratory test results and results of neuropsychological tests and medication.

### 2.4. Evaluation of Neuropsychiatric Symptoms

Each participant underwent an evaluation at baseline and at the 6-month follow-up. The evaluation consisted of the following tests, the Geriatric Depression Scale (GDS) for the detection of depressive symptoms.<sup>33</sup> The official translation into Greek and access <https://web.stanford.edu/~yesavage/GDS-Greek.html>.<sup>34</sup> The Hamilton Depression Scale (HAM-D)<sup>30</sup> used to assess patients' emotional state through 17 questions from the caregiver's perspective and the Neuropsychiatric Inventory<sup>35</sup> for the detection of neuropsychiatric disturbances.

### 2.5. Cognitive Training Program

The online Memory Motivation (MeMo) application is designed to meet the needs of patients with mental disorders, health professionals involved in cognitive impairment prevention and cognitive activation, and people who want to exercise their memory and attention.<sup>18</sup> The MeMo program was implemented by a team of health professionals from the Institut Claude Pompidou, Association IA, CoBTeK lab, Université Côte d'Azur, Nice, France and was translated into Greek by the University Department of Neurology of the Democritus University of Thrace, after the relevant of its creators. The program consists of recreational activities and exercises aimed at strengthening and practicing cognitive functions. It includes three main categories: memory, adaptability and attention. Each exercise was

designed to train a specific cognitive function in order to allow individualized training according to their deficits. The exercises have grading levels of difficulty and store each user's personal scores and progress assessment. Each time users receive the highest score in a level, they change level automatically. Once an account is created, users can monitor the progress of their performance in the exercises. This also allows therapists to monitor the patient's performance over time. Available for free at the following link: <http://www.memory-motivation.org/home-4/> in all three languages available.

## 2.6. Procedure

Each training session included the MeMo program, lasting 20-30 minutes once a week for 6 consecutive months, which was the same for all participants and conducted by the same researcher. All interventions were individualized and electronic equipment was available to execute the computerized cognitive training programs. A laptop with a touch screen was mainly used, as it seemed that the use of a computer mouse burdened the performance in timing tests, while the use of tablets was considered insufficient due to the small screen. Prior to joining the program, two computer programming sessions were conducted. Each participant had the opportunity to leave during the intervention, if they wished. The intervention program was held face-to-face in an outpatient "Memory School", which is developed by the University Department of Neurology and the logistical equipment required was available and common to all. Thus, possible problems such as not availability of the necessary resources (i.e., computer device, wifi) were omitted".

The introduction of the 50 participants in the study was done in staggered time periods, as the whole process of implementing the program was done by one researcher, a key element to avoid drop-outs.

## 2.7. Statistical Analysis

All data were analyzed using SPSS statistical software (version 27.0) was used; all data are presented as mean±SD. Parametric tests were performed because all variables followed a normal distribution. Significant differences ( $p > 0.05$ ) were found using a two-way repeated ANOVA (time × condition) to determine the differences in (a) GDS, (b) NPI, and (c) HAMILTON. The post hoc multiple comparisons were performed by using Bonferroni correction. Significant was accepted at  $p < 0.05$  for all measures.

## 3. RESULTS

A total of 100 participants (27 males, 27.0%), with a mean age of 69.92±7.44 years and mean duration of education of 9.48±4.96 years, were tested. The demographic and clinical characteristics of control and experimental group are given in Table 1. Male sex was

more frequent in control group (32%), while female in experimental group (78%). The age of the participants was similar between control; <65 years (28%), 66-74 (42%) and >75 years (30%) and experimental group; <65 years (18%), 66-74 (52%) and >75 years (30%).

### 3.1. Results in Emotional Domains

In the experimental condition, a significant decrease was found in the GDS test ( $p < 0.001$ ; 3.00±1.70 to 2.10±1.22), the NPI test ( $p=0.043$ ; 1.42±1.58 to 1.10±1.31) and the HAMILTON test ( $p < 0.001$ ; 4.52±1.90 to 3.18±1.48) compared to the control condition. (Table 2 & Figure 2)

### 3.2. Results in Cognitive Domains

No significant change was found in the MoCA test (range=25.04±1.96 to 24.90±3.02), CAMCOG test (89.48±7.20 to 4.1 88.34±8.10) and MMSE (27.62±1.50 to 27.56±1.45) in the experimental condition (Table 3).

Figure 2. Mean scores of tests between two evaluations

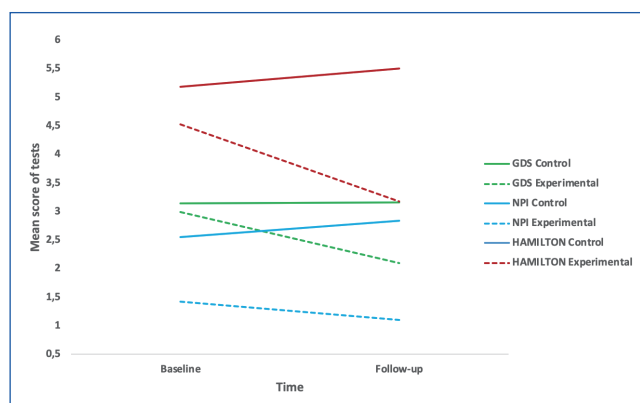


Table 2. Measures of tests following the control and experimental conditions

Measure	Condition	Baseline (Mean±SD)	Follow-up (Mean±SD)
GDS	Control	3.14±2.51	3.16±2.40
	Experimental	3.00±1.70	2.10±1.22*
NPI	Control	2.56±2.55	2.84±2.57
	Experimental	1.42±1.58	1.10±1.31*
HAMILTON	Control	5.18±4.00	5.50±3.87
	Experimental	4.52±1.90	3.18±1.48*

\*P < 0.05 compared to baseline and control condition.

Table 3. Measures of cognitive tests following the control and experimental conditions

Measure	Condition	Pre (Mean±SD)	Post (Mean±SD)
MOCA	Control	24.40±2.15	22.58±2.41
	Experimental	25.04±1.96	24.90±3.02
CAMCOG	Control	87.66±7.12	85.22±8.83
	Experimental	89.48±7.20	88.34±8.10
MMSE	Control	27.80±1.44	27.52±1.87
	Experimental	27.62±1.50	27.56±1.45

#### 4. DISCUSSION

The results of the implementation of the personalized cognitive training program indicated a statistically significant decrease in the experimental group in the neuropsychiatric symptoms. This finding is in accordance with previous studies, which emphasized the role of cognitive training on improving cognitive and behavioral symptoms.<sup>11,14</sup> In the meta-analysis of research for the investigation of non-pharmacological interventions, physical exercise is proposed as an effective intervention for cognitive empowerment, while for the improvement of neuropsychiatric symptoms, computerized cognitive education is considered as an effective strategy.<sup>37</sup> In contrast to the systematic review carried out by Liang et al.,<sup>38</sup> 18 studies confirmed that this type of intervention is considered the most sustainable for improving the cognitive status of the elderly with MCI, giving statistically significant results in general cognitive functionality and memory, but not in executive function. Similarly, the findings of other studies<sup>14,17,39,40</sup>, as well as a systematic review of 32 studies that highlighted short-term and long-term benefits of cognitive interventions.<sup>41</sup> The decrease of depressive symptoms has also been confirmed by the meta-analysis of cognitive interventions<sup>7</sup>, which also found that people with MCI had long-term benefits in memory and depression.

At this point we present the methodological design and some key points that proved to be the strengths of the research. The study provides useful information about the necessary duration of training. The number of 24 sessions for each participant (total 36 hours) of the present study has not been clarified in the literature if it is sufficient time for long-term results. The "dose effect" of cognitive intervention is a field that has been explored to find out whether there is a correlation between the effectiveness of the intervention and the cognitive game time or the number of game sessions.<sup>42-44</sup> It is not always proven that the duration of each session and the number of total sessions are positively related to the cognitive and emotional impact on individuals with MCI. There are studies with more sessions and longer duration of total sessions, but with smaller results sizes.<sup>7</sup>

Another important element that has been reported in previous studies<sup>15,45</sup> is the motivation for participating in training programs. Motivation is a key element in the theory of programs in older adults with cognitive impairment.<sup>46,47</sup> Within the motivational component of this program, two key mechanisms (perceived benefit and support) were shown to influence the extent to which an older adult with cognitive impairment is motivated to undertake an exercise-based intervention. The MeMo program was designed to increase intrinsic motivation to continue exercising thanks to several features. First, the game interface

was designed specifically for the target population of cognitively impaired older adults (i.e., simplified graphical user interface, simplified instructions with regular reminders, and clear game rules) and thus was easily usable by the participants in this study. In addition, the difficulty level of the exercises was dynamically adjusted to the performance of the participants in order to provide an error-free type of training and to keep the participant in a "challenge zone". Finally, it was implemented on a touch screen computer to reduce the limitations associated with the use of unfamiliar technological interfaces such as mouse and keyboard, which are often considered difficult to use by the elderly.<sup>16</sup> These elements also explain the minimal drop-out of the participants.

Another aspect is the implementation of the intervention program, which included exclusively individual sessions with each participant and a personalized program, components that have been shown to be useful for the effectiveness of such interventions<sup>48,49</sup>, while there are also research data that support the superiority of group interventions.<sup>50,51</sup>

Hence, the methodological limitations of the study are i) it was not designed to examine the duration of the benefits of the interventional program, a parameter which in the literature research has shown to provide interesting data in neurocognitive disorders ii) the small sample size reduces the generalizability of the results and might also have limited the intervention effects, iii) in aged populations familiarity with the use of computer is limited, a barrier that was overcome with constant guidance from the researcher, iv) subtypes and causes of MCI were not adjusted for in the analysis.

#### 5. CONCLUSION

The personalized cognitive training program for people with MCI appeared to create a pattern of reduction in neuropsychiatric symptoms. Multidimensional cognitive education is an important tool for healthy cognitive aging and the prevention of dementia, contributing to the literature of suggested non-pharmacological interventions. The results could be used in future clinical practice of prevention of neurocognitive disorders. Future studies should aim to identify potential biomarkers of effects on cognitive education, which may increase our understanding of the mechanisms based on cognitive enhancement and neuroplasticity of the brain, which may be useful in predicting the effectiveness of interventions.

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