Managing Cognitive Decline through Social Robot-Based Intervention: The Study Protocol of a European Randomized Controlled Trial

Giulio Amabili, Elvira Maranesi, Arianna Margaritini, Anna Rita Bonfigli, Elisa Felici, Federico Barbarossa, Marco Benadduci, Laetitia Gosetto, Julie Guebey, Terje Grimstad, Riitta Hellman, Andrei Iulian Marin, Lars Thomas Boye, Ionut Manuel Anghel, Tudor Cioara, Roberta Bevilacqua

Submitted to: JMIR Research Protocols
on: October 16, 2024

Table of Contents

Managing Cognitive Decline through Social Robot-Based Intervention: The Study Protocol of a European Randomized Controlled Trial

Giulio Amabili[1]; Elvira Maranesi[1]; Arianna Margaritini[1]; Anna Rita Bonfigli[1]; Elisa Felici[1]; Federico Barbarossa[1]; Marco Benadduci[1]; Laetitia Gosetto[2]; Julie Guebey[2]; Terje Grimstad[3]; Riitta Hellman[3]; Andrei Iulian Marin[4]; Lars Thomas Boye[5]; Ionut Manuel Anghel[6]; Tudor Cioara[6]; Roberta Bevilacqua[1]

[1]Scientific Direction IRCCS INRCA Ancona IT
[2]Division of Medical Information Sciences HUG Geneva CH
[3]KARDE AS Oslo NO
[4]IRIS robotics Iasi RO
[5]TELLU AS Oslo NO
[6]Technical University of Cluj-Napoca Cluj-Napoca RO

Corresponding Author:
Elvira Maranesi
Scientific Direction
IRCCS INRCA
via S. Margherita, 5
Ancona
IT

Abstract

Every year in Europe the number of diagnoses of dementia increases significantly. Dementia is challenging the society in terms of quality of life, costs of healthcare systems and caregivers' burden. Dementia is often preceded by a status of mild cognitive impairment (MCI), during which healthy lifestyle and cognitive therapy seem to be effective in counteracting the decline. The engAGE project aims to build a technological platform to counteract cognitive decline in people with MCI through both cognitive therapy and lifestyle management. The platform is built around the social robot Pepper, which provides cognitive therapy weekly at healthcare or daycare facilities. In addition to the social robot, a mobile app and an activity tracker are integrated within the platform to help older people with MCI to monitor their sleep and physical activity, other than offer cognitive games at home. All the data gathered from the three devices flow via-cloud into the platform to be analyzed by a machine learning (ML) algorithm aimed to predict the ongoing of cognitive decline. The proof of concept of the engAGE platform is a 6-months long randomized controlled trial (RCT) aimed to test the solution in three European countries: Italy, Switzerland, and Norway. The primary interest of the study is to assess the impact of the engAGE platform on cognitive capacity through quantitative and standardized scales. In addition, changes in social engagement and quality of life are measured. Then, the proof of concept also focuses on the acceptability and usability of the platform, evaluated through the SUS scale and the UTAUT questionnaire. The proof of concept, is an innovative study focused on the impact of a technological-based intervention designed for older people with MCI, that aims to tackle directly the cognitive decline through cognitive training, and indirectly through the improvement in terms of quality of life, social engagement, physical activity and sleep quality of primary end users.

(JMIR Preprints 16/10/2024:67601)
DOI: https://doi.org/10.2196/preprints.67601

Preprint Settings

1) Would you like to publish your submitted manuscript as preprint?

✓ **Please make my preprint PDF available to anyone at any time (recommended).**
Please make my preprint PDF available only to logged-in users; I understand that my title and abstract will remain visible to all users.
Only make the preprint title and abstract visible.
No, I do not wish to publish my submitted manuscript as a preprint.

2) If accepted for publication in a JMIR journal, would you like the PDF to be visible to the public?

✓ **Yes, please make my accepted manuscript PDF available to anyone at any time (Recommended).**

Yes, but please make my accepted manuscript PDF available only to logged-in users; I understand that the title and abstract will remain v
Yes, but only make the title and abstract visible (see Important note, above). I understand that if I later pay to participate in <a href="http

Original Manuscript

Managing Cognitive Decline through Social Robot-Based Intervention: The Study Protocol of a European Randomized Controlled Trial.

Abstract

Every year in Europe the number of diagnoses of dementia increases significantly. Dementia is challenging the society in terms of quality of life, costs of healthcare systems and caregivers' burden. Dementia is often preceded by a status of mild cognitive impairment (MCI), during which healthy lifestyle and cognitive therapy seem to be effective in counteracting the decline. The engAGE project aims to build a technological platform to counteract cognitive decline in people with MCI through both cognitive therapy and lifestyle management. The platform is built around the social robot Pepper, which provides cognitive therapy weekly at healthcare or daycare facilities. In addition to the social robot, a mobile app and an activity tracker are integrated within the platform to help older people with MCI to monitor their sleep and physical activity, other than offer cognitive games at home. All the data gathered from the three devices flow via-cloud into the platform to be analyzed by a machine learning (ML) algorithm aimed to predict the ongoing of cognitive decline. The proof of concept of the engAGE platform is a 6-months long randomized controlled trial (RCT) aimed to test the solution in three European countries: Italy, Switzerland, and Norway. The primary interest of the study is to assess the impact of the engAGE platform on cognitive capacity through quantitative and standardized scales. In addition, changes in social engagement and quality of life are measured. Then, the proof of concept also focuses on the acceptability and usability of the platform, evaluated through the SUS scale and the UTAUT questionnaire. The proof of concept, is an innovative study focused on the impact of a technological-based intervention designed for older people with MCI, that aims to tackle directly the cognitive decline through cognitive training, and indirectly through the improvement in terms of quality of life, social engagement, physical activity and sleep quality of primary end users.

Trial Registration: The study was recorded in ClinicalTrials.gov on the number NCT06302686. The study was approved by the Ethic Committee of the IRCCS INRCA in Italy (protocol number: 6293/2023) and by Canton Commission of Etihics and Research (Commission cantonale d'éthique de la recherche – CCER) in Switzerland (project ID: 2023-00774).

Keywords: older people; mild cognitive impairment; social robotics; technology for elderly; digital health; cognitive training; innovation in healthcare.

Introduction

Background

Dementia is a chronic neurodegenerative syndrome characterized by deficits in cognitive functions, associated with the loss of daily function and with mental and behavioral disorders. There are over one million people with dementia in Italy, of which 54% are due to Alzheimer's disease and about 16% to vascular dementia [1]. The Swiss Federal Office of Public Health expects an increase of people diagnosed with dementia to over 190.000 individuals by the year 2030, and to almost 300 000 by 2060 [2]. The same trend is expected in Norway, where the number of persons with dementia was estimated to more than double from 2020 to 2050 [3]. According to literature, cognitive interventions [4], regular physical activity [5,6] and reminiscence therapy appeared effective in the therapy of people with mild to moderate dementia. Cognitive stimulation programs, computerized individual cognitive training, as well as physical exercise appear to be able to induce a significant improvement in cognitive performance, quality of life and well-being in people with mild to moderate dementia [7-9]. Several studies show that, especially in the early stages of the disease, stimulation and participation in various types of activities can help to counterbalance the cognitive changes related to the pathology thanks to cognitive plasticity [10,11]. Neuro-cognitive disorders, in particular dementia, represent a major challenge for the society. Efforts to reduce the burden for caregivers, as well as for the society at large are imperative. Older people generally report higher preferences for their home over other living arrangements and from the societal point of view this can contribute to burden of care, e.g. for their families. Dementia caregivers are at high risk of care burden, anxiety and stress, which exposes them to a higher rate of mortality compared to non-caregivers [12]. Thus, promoting ageing in place for people with dementia should not constitute a strategy to shift the burden of care from the formal care services to the informal caregivers. Instead, efforts should focus on reducing caregiver stress. Part of the difficulties and stress related to caregiving might be prevented by new Information and Communication Technologies (ICT) and by developing innovative support services for these people. The introduction of innovative and cost-effective interventions to reduce the burden of dementia on public finances and individual families should be envisaged.

The engAGE project

In this scenario, the engAGE (Managing cognitivE decliNe througH theatre therapy, Artificial intelligence and social robots drivEn interventions) project – co-financed by the Ambient and Assisted Living (AAL) programme of the European Union [13] – aims the to counteract and slow down cognitive decline progression, to enhance the intrinsic capacity of the users, and to support the wellbeing of older persons with mild cognitive impairment (MCI) by providing an ecosystem of services based on an innovative system that integrates social robots, mobile apps, and wearable sensors. Moreover, the engAGE project combines home-based intervention (daily usage of mobile app and wearable fitness tracker) with the group cognitive training at healthcare facility (weekly social robot-driven sessions). Thus, engAGE targets the following challenges and needs for older people with MCI, informal caregivers (family members), and formal caregivers (healthcare professionals). The project is primarily focused on older people with MCI, aiming to improve their quality of life and well-being, allowing them to preserve their identity, to reduce stress, memory loss, or communication challenges. The social robot can be a great tool in engaging older adults in this kind of activities. It is always available and able to provide verbal clues or suggestions according to older adult's wishes, needs and memories. Moreover, the social robot may coach the older adults to perform daily activities with greater independence (i.e. coaching stepwise prompting to complete activities in-home) and support to caregivers as well. Since caring for people with MCI puts a significant burden on informal caregivers, having the support of a technological platform can reduce anxiety, worries, and stress. The caregivers can personalize the content of interventions to the wishes and preferences of the older adults.

Goal of the study

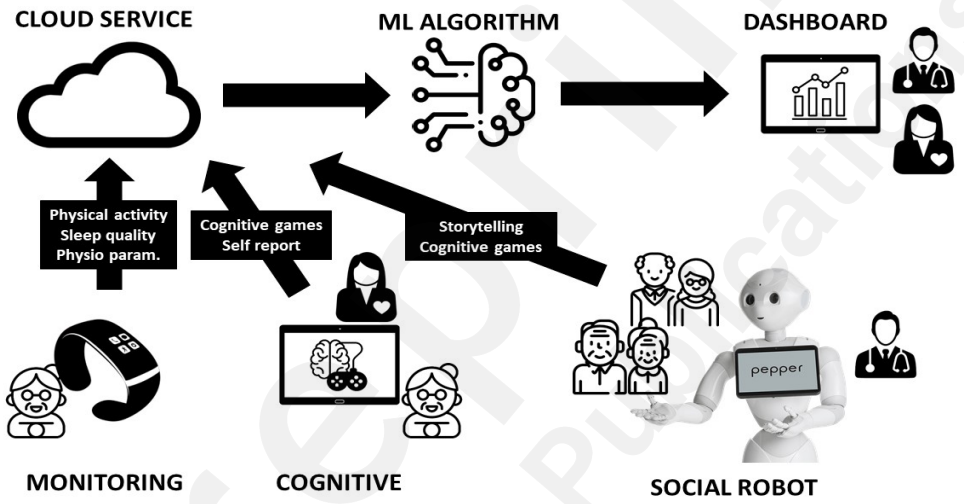
This paper aims to present the engAGE project study protocol, which consists of a 6 months long randomized control trial (RCT) in real scenario in 3 European countries (i.e. Italy, Switzerland and Norway) in order to provide an up to date those researchers, scientists and stakeholders interested in the use of social robotics and ICT technologies in healthcare and digital health. The novelty of this study design is given by the combination of at-home and in place intervention to maximize the impact of cognitive stimulation through technology, minimizing the caregivers' burden, but encouraging the social connectedness among end users and with the care network. Finally, the paper discusses in deep the ethical issues concerning the adoption of social robotics, machine learning algorithms, and health data management of older adults with mild cognitive impairment, along with the long-debated question about the informed consent signed by people with MCI.

Methods

The engAGE platform

The engAGE system offers four main services built around a social robot for self-managing and sustaining the cognitive function of older adults with MCI [14]: holistic monitoring of daily life activities and perceived health state and wellbeing; assessment of cognitive state and potential decline by leveraging on Machine Learning (ML) algorithms; social robot based cognitive function support and coaching using cognitive games and storytelling scenarios; communication, cognitive stimulation and personalization platform for end-users. Fig. 1 schematizes the engAGE platform services with the integration of social robots, sensor-based monitoring, and ML techniques. The primary end users (older adults) mainly interact with three devices: the Pepper social robot, a tablet, and a fitness tracker wearable device (Fitbit). The formal caregivers supervise the execution of end-users' activities and help them when needed. The interaction is done through the devices associated dashboards.

Figure 1. The engAGE platform



The Social Robot Service

On the social robot service, the Android version of Pepper's tablet offers dashboards for cognitive games, storytelling, and activities to the end-user through an easy-to-use interface. Equivalent cognitive games are also integrated into the communication service to allow the end-user to play them at home on the tablet. Pepper is a humanoid social robot able to dialogue with the user by speaking, moving, and expressing emotions being also equipped with an Android tablet placed at its chest. The user logs through the tablet at every session, then (s)he interacts with the robot and plays the planned activities (drama play or cognitive games). To track the user's progress, each performance is recorded, and scores are sent to the cloud along with the user ID. As the sessions are held in group of 4 or 5 older people, the users can choose to play individually or in teams. Once the type of game is selected, the user is redirected to a new screen in which all the games corresponding to the type selected is displayed. When the user is playing and succeeding a task, the robot congratulates with him/her. To be sure that the user understands what the robot says, the words are displayed on the screen like subtitles. The interaction is recommended to be vocal as much as possible to improve the user experience. Different categories of cognitive games and storytelling activities are implemented in the service. The games are and will be iteratively developed and included in the service in the different versions of the prototype while considering end-users' feedback:

- Familiar games: crossword, memory card, and remember the appeared objects.

- Quizzes: picture, musical and cultural quizzes.
- “Story/play telling: story listening, plays poems reciting and YouTube shorts; then it asks questions about.

The Communication Service

The communication service is the hub of the whole system for providing the dashboards for end-user interactions at home. It is a web application with several dashboards in which all the end-users’ categories can communicate through. This service is based on the MEMAS Life Mastering Assistant having the following functionality which helps people with MCI: calendar with reminders, step by step instructions for daily activities in form of series of images with spoken comments or videos, radio channels easy to access via streaming, photos with spoken comments and videos, music, easy access to network newspapers, cognitive games, weather forecasts, self-reporting questioners, graphical results from the ML algorithms for the secondary end-users. The service is usable by both primary and secondary users. The primary user can be connected to several secondary users. In the administration module (a website page), the secondary user (i.e. family member or formal caregiver) can manage an activity calendar, build albums with photos and videos, configure access to favorite radio channels and newspapers. In general, the secondary user can edit the primary user’s interface to make the use of the service as simpler as possible and tailored to the primary user’s needs. Data regarding self-assessment and cognitive games scores are sent to the ML service for further analysis. Also in this service, the games are and will be iteratively developed and included in the service in the different versions of the prototype while considering end-users' feedback: Sudoku, mahjong, minefield, crosswords, logics, math, hangman, and memory card.

The Monitoring Service

The monitoring service offers a tablet-based application where the parameters such as heart rate, sleep status, physical activity (steps and walked distance) are monitored. This data are further used by the ML service as input for its algorithms. The monitoring service has little user interaction outside of the use of sensor devices. This service features a mobile application gateway which transfers data from sensor device (Fitbit) into the cloud. In the first iteration, it transfers Fitbit data from the Fitbit service. It does so automatically while running in the background on the mobile device (Android tablet) of the primary user. Once the login and Fitbit authentication has been established, the app runs in the background, regularly polling data from the Fitbit service.

The ML Analytics Service

The ML analytics service has no direct end-user interaction, it gets data from the monitoring service and the communication platform and provides the results to be displayed in the latter. The main goal of the service is to assess and correlate the daily physical activity, sleep parameters, games scores and self-assessment data to offer a view of MCI progress [15]. It combines deep neural network algorithms/models to analyze objective activity data coming from Fitbit wearable device with graph learning techniques that captures structural insights from subjective self-reporting activities to construct a better understanding of symptoms associated with cognitive decline.

The study design

The proof of concept is conducted as a controlled longitudinal pilot study, with a before and after design where the observations are made on a series of enrolled individuals, receiving the intervention described below with control group, with data collected before and after the installation and use of the technical solution. The goal of trial evaluation is to assess the engAGE technology integration into everyday life, effectiveness on the cognitive decline, acceptance over six months, as well as security and reliability of proposed solutions.

In Italy, the end-users are recruited from the Neurology Unit and Alzheimer Assessment Unit (Memory Clinic) and from the Alzheimer day-care centre of the IRCCS INRCA. The research team has the possibility to communicate with potential participants of previous projects and initiatives, as well as with other people who might be interested in contributing to the project evaluations. This method makes possible to be in contact with clients met before and with whom a relationship of trust has been already established.

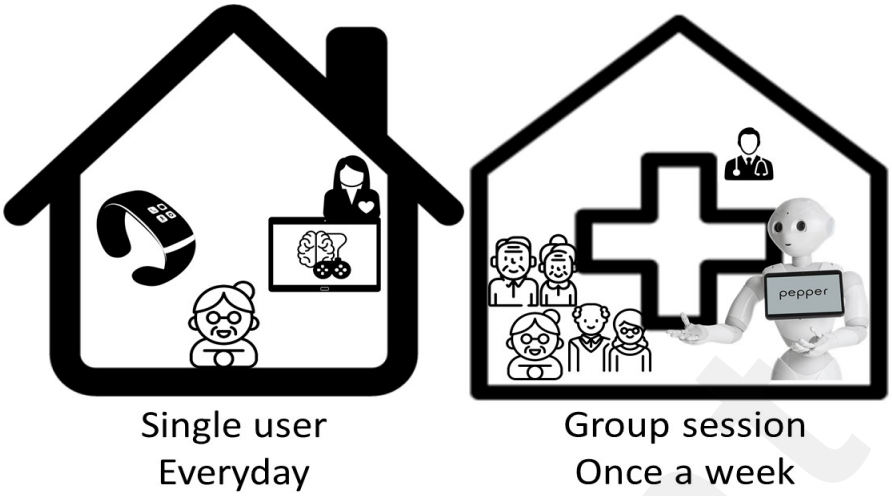
In Switzerland, the end-users are recruited with the help of a home assistance and care institution (IMAD). The research team also reaches the partner patient program for participants with potential MCI. All seniors interested in the study are considered for participation.

In Norway, participants are recruited at two day-care and housing centres in the city of Arendal. Solhaug is a day-care centre for old residents living in their own homes, while the second one, Plankemyra, is a combined housing and day-care centre.

The experimental group

The experimental group (EG) use the engAGE system in two different settings: at healthcare organization and at home. For the Italian site, the healthcare organization consisted of the Neurology Unit and Alzheimer Assessment Unit (Memory Clinic) and from the Alzheimer day-care centre of the IRCCS INRCA. The weekly sessions are run at the IRCCS INRCA usability lab (YOUSE), placed within the hospital. For the Swiss site, the recruitment is via the Geneva homecare Institution (IMAD), where the participants are tested. If they result compliant to the inclusion and exclusion criteria, they attend the weekly sessions at the Geneva University Hospital's living lab (HUG). For the Norwegian sites, both the recruitment and the weekly sessions are managed by the aforementioned day care centres in the city of Arendal. At the healthcare organization, the primary end user interacts with Pepper. The interaction at healthcare organization is supervised by tertiary end user (formal caregivers, i.e. occupational therapist, psychologist, nurse, etc…) and includes the following activities: dialoguing with the robot, storytelling, drama play, cognitive and physical games. This interaction is planned to last about 1 hour and to be scheduled once a week for 6 months. At his/her home, the older user interacts with the tablet and is supervised by the relative informal caregiver. Also in this case, the user plays cognitive and physical games installed on MEMAS app. This activity is suggested to be performed for 0.5 hour, every day for 6 months. Throughout the whole period of experimentation (unless (s)he decides otherwise), the older user wears the smartwatch that measures his/her physiological parameters and the steps. Any activity performed by the seniors is assigned by formal caregiver and can be personalized considering the user's abilities (difficulty levels of the games), lifestyle (reminding and monitoring services), and social interactions. In the picture below (Fig. 2), the intervention for EG is schematized.

Figure 2. Experimental group study design



The control group

The control group (CG) is provided with a booklet, where cognitive games are illustrated. Moreover, suggestions on how to live a healthy and active ageing are provided. At the beginning of the trial, the participants of CG are invited to follow the booklet, fulfil the cognitive games and follow the advice, but are neither motivated nor contacted during the experimentation, unless they wish otherwise.

The RCT phases

The proof of concept procedure is divided into three different phases, after the recruitment of the participants: Baseline evaluation (T0), Mid-term evaluation (T1, after three months from T0) and Final evaluation (T2, after six months from T0), with the aim of collecting data as described in Textbox 1:

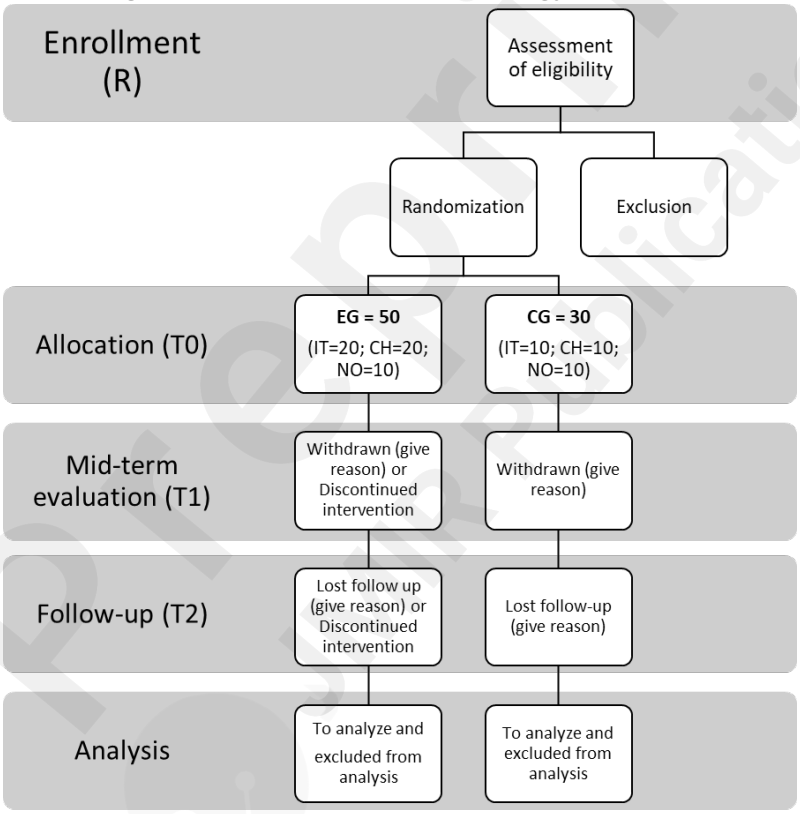
Textbox 1. Proof of concept phases.

1. Recruitment phase: the recruitment protocol includes general information on the subjects, in particular, health status and cognitive condition. The information is collected with the help of the caregiver/family member if needed.
2. Baseline evaluation consists of the first real contact with the users and their families, before the start of the proof of concept.
3. Second evaluation (after three months of use): the aim of mid-term evaluation is to collect useful information on the use of the engAGE platform after a short period of use for detecting and analyzing the technology acceptance and usability issues. Obviously, the CG is not evaluated at this stage.
4. Final evaluation (after six months of use): the aim of this phase is to collect useful information on the whole benefits perceived by the users after a meaningful period of use of the system. The final evaluation is conducted after the system de-installation, to detect and analyze the impact of the system in the daily life of the older people and their family.

Recruitment

A certain number of people are recruited for the study, then those who do not meet the criteria or decline the participation are excluded. The remaining participants are randomly assigned to the EG or to the CG. The randomization technique, conducted by a statistician, based on a single sequence of random assignments is used. A list of random numbers generated by the computer is used and subject is assigned a number based on their order of inclusion in the study. According to this technique, in Italy and Switzerland the 30 subjects are randomly assigned to one of the 2 study groups (20 in EG and 10 in CG), while in Norway 20 subjects are equally assigned to the two groups. Then, for both the groups it must be taken note of who loose follow up, discontinued intervention, and/or are excluded from analysis. The procedure is summarized in the figure below (Fig. 3)

Figure 3. Recruitment methodology flowchart



Older people with MCI

Once the informed consent is obtained in duplicate, the compliance with the criteria of inclusion and exclusion of the study are verified and the baseline evaluation is carried out with the questionnaires.

Textbox 2. Inclusion and exclusion criteria for people with MCI.

The inclusion criteria are:

1. Aged 65 years and over.
2. Capacity to consent.
3. Already diagnosed with MCI.
4. Global Deterioration Scale (GDS) [16] <1.

5. MoCA score [17] between 21 and 25.
6. MAC-Q [18] ≥ 25.
7. Reisberg scale [19] between 2 and 4.
8. Clinical Frailty Scale score [20] between 1 and 3.
9. Having an informal/formal caregiver to support in carrying out the main daily activities.

The exclusion criteria are:

1. Failure to meet the inclusion criteria.
2. Concomitant participation in other studies.
3. Lack of written informed consent.
4. Significant visual or hearing impairment.

Informal caregivers

Informal caregivers are mostly family members or daily references of the people with MCI. Connections between informal caregivers and clients are private and not via a care organization. Informal caregivers are concerned about the well-being of the people with MCI and they provide emotional or practical support regularly. Although it is easier to live nearby the patient, informal caregivers do not necessarily need to live close by him/her. Informal caregivers are included in the engAGE project since they play an important role in the daily life of the people with MCI. Moreover, the informal caregivers can fulfil caring tasks to reduce the burden of formal caregivers. A good collaboration between informal caregivers and formal caregiver is needed as the informal caregivers can be the link between the client and the formal caregiver.

Textbox 3. Inclusion and exclusion criteria for informal caregivers.

The inclusion criteria are:

1. Being the informal caregiver of an old person with MCI.
2. Availability of time to participate.
3. Visit the assisted person at least two times a week or live with him/her.

The exclusion criteria are:

1. Failure to meet the inclusion criteria.
2. Concomitant participation in other studies.
3. Lack of written informed consent.

Formal caregivers

Care professionals or formal caregivers are professionally responsible for dementia care. They are trusted agents for people with MCI and have direct contact with older adults and provide care when needed.

The formal caregivers are case manager, neurologist, psychotherapist, occupational therapist, and nurse. The case manager is responsible of the organization. The neurologist is a specialized medical doctor who diagnoses the disease and prescribes the treatment. The psychotherapist leads the intervention, whereas the nurses and the occupation therapists act as assistant. These professionals may be especially found in day care, but they are available in residential home care as well.

Textbox 4. Inclusion and exclusion criteria for formal caregivers.

The inclusion criteria are:

1. Over 1-year experience.
2. Psychologist, neurologist, occupational therapist, nurses from health care facilities or paid by the participants.
3. Availability of time to participate.

The exclusion criteria are:

1. Failure to meet the inclusion criteria.
2. Concomitant participation in other studies.
3. Lack of written informed consent.

Outcomes

The proof of concept aims to assess the feasibility of using the engAGE platform as a support tool to counteract cognitive decline in older people with MCI. For this reason, the primary interest is to assess the impact of the engAGE platform on cognitive capacity. Secondarily, the study also focuses on the impact on social dimension and quality of life, as well as usability and acceptability of the platform. All the outcomes are presented in Table below:

Table 2. Tools and dimensions of the primary end users' protocol.

Outcome(s)	**Clinical assessment**
Perceived stability of cognitive status by the older adults	MAC-Q [18]
Acceptability of the engAGE platform	UTAUT [21]
Social connectedness of older people	UCLA [22]
Reduction of the caregiver burden of formal and informal carers	ZARIT [23]
Adherence to intervention	Ad hoc questionnaire
Well-being of the informal caregivers	WEMWBS [24]
Quality of life of the older people	EQ-5D-5L [25]; QoL-AD [26]
Usability and affordability of the solution of the informal caregiver	SUS [27]
Improving quality of work of the formal carers	Ad hoc questionnaire

Data analysis

The different types of data that are collected in the engAGE project are:

- Credentials - usernames, passwords, email addresses and similar security information used for authentication and account access in different services of the platform.
- Personal data such as first name, last name, gender, age, weight, height, email address, contact address, phone number, etc. of older adults' end-users in different services of the platform.
- Answer to specific questions in self-assessment questioners on MEMAS.
- Games score from the Pepper applications.
- Measurements and monitored parameters such as weight, heart rate, blood pressure, physical activities of older adults' end-users gathered through the monitoring infrastructure.
- Historical data about the above measurements and monitored parameters for training and using ML algorithms for each older adult in the ML service.

In the engAGE testing and evaluation phase, the following data are processed:

- Information and results from questionnaires.
- Cognitive games scores.
- Historical data for each end-user collected measurements.
- Any information the end-users decide to share through discussions / interviews as well as data providing feedback from trials.

The first step of the data analysis deals with the description of the sample. Continuous variables are reported as either mean and standard deviation or median and interquartile range on the basis of their distribution (assessed using Kolmogorov-Smirnov test). Categorical variables are expressed as an absolute number and percentage. Mann-Whitney U tests (for non-normal distribution), or Chi-Square tests (normal or non-normal) are used to compare the independent and dependent variables between the pre- and post- conditions, in addition to simple descriptive statistics (means, medians and standard deviations as appropriate).

In order to verify the achievement of the primary endpoint (i.e., MAC-Q), subscales of the questionnaire are calculated. Means and standard deviation or medians and interquartile ranges of the scores are reported according to their distribution. Correlation coefficients (Pearson for normally distributed variables, Spearman for non-normally distributed variables) of the sub-scales with the other rating scales at each stage of the study and with the main characteristics of the subjects arecalculated to check for potential determinants of higher acceptability.

Ethics

To guarantee the observance of ethics, the principles of the Declaration of Helsinki [28] and Good Clinical Practice guidelines are adhered to, and the study is initiated following receipt of an evaluation and approval of the study by national independent ethical boards.

Ethical issues

Technological dependence, especially on AI technologies, represents a major ethical dilemma today for scientific community. To limit the risk, the European Commission’s international programmes have introduced guidelines for conducting studies that require the introduction of a new technology,

called Responsible Innovation [29]. The core principles of Responsible Innovation are also applied within the engAGE project. A strategy underlying the prevention of technological dependence is including different actors around the older people, in the process of acquiring skills and daily use of technology. In this way, technological solutions such as those proposed by engAGE, respond to the definition of socio-technological system rather than technological, since they are placed in a care context that does not involve the replacement of the caregiver but stimulates the user to play a leading role in the management of their health.
The services proposed are intended to support the maintenance or improvement of cognitive abilities through specific activities and do not replace (in whole or in part) the support from professional services.
During the installation of the technology, moreover, information is provided to the caregiver about the limits of the technology, which can in no way replace the role of the familiar and formal assistant, but only assist in some activities.
During the use of robotic platforms or, more in general of technological applications, a general difficulty in distinguishing between artificial world and reality, may occur. Especially, in case of vulnerable populations as the older people, the interaction may generate a general feeling of attachment and dependency. To avoid this, engAGE has been designed to not look as a human, but to preserve artificial aesthetics, as suggested by the guidelines [30]. In addition, during the first contact with the participants but also during all the intervention, researchers are in contact with the users, continuously stimulating the awareness about the technological applications, as well as monitoring the appropriateness of the use of the solution in terms of autonomy of the users, specific needs and personal preferences. Following the recommendations provided by the Italian Bioethics Board (Comitato nazionale di bioetica, Cnb) of the Italian Ministry of Health [31] on robotics and roboethics, the exit strategy of engAGE aims to:

1. Promote an adequate experimentation of robotics in the field assistance to ensure conditions for physical and psychological integrity of the user, explaining the risks and benefits, highlighted also in the informed consent.
2. Ensure both equitable access to robotic and general technologies and the use of robot to assist and not to replace humans, to avoid delegating the irreplaceable human task of care and assistance to the machine.
3. Demonstrate that the introduction of robotics in medicine entails always the real consideration of the benefits, of the complexity of the change complete with the structure of the services and the economic burden that this entails.

Users who take part in the study do not incur any direct or indirect costs related to the use of the technology platform. The platform is provided to the subjects by the pilot sites and must be returned to the research team at the end of the trial.

Informed consent for people with MCI

Participants in this study provide written informed consent, even though the acquisition of informed consent from people with MCI is a long-debated issue. Although degenerative neurological syndromes over time lead to a progressive decline in cognitive functions and with them the ability to express valid consent, the diagnosis of Alzheimer's disease or MCI does not in itself lead to the loss of this ability. The legal capacity and the capacity to act remain, unless proven otherwise, from the age of majority until the death of the person. In fact, only a judicial measure can protect the person with MCI who is unable to provide informed consent by appointing a legal representative. From a neuropsychological point of view, the impairment of executive functions (abstraction ability, problem solving, judgment and criticism, planning, planning, farsightedness, 'decision making' ...) is directly proportional to the decrease in capacity both in a general sense that in the various fields: health and economic decisions, driving skills, etc. However, these cognitive functions can be spared in the early

stages of the disorder (MoCA score 21-24), unlike others that are affected early, such as memory and orientation. It is also common clinical experience that, even if unable to understand the contents of a standard "informed consent" form (which must certainly be simplified), the person with MCI is often able to express his/her choices in line with his lifestyle, preferences and values. This underlines the importance of preserving the possibility for potential participants to use their skills to share possible choices.

Informed consent is a legal condition in which a person accepts an action that is proposed to him/her (in our case, active participation in the feasibility study). To be "informed", consent must be based on a full understanding of the action itself and the implications it can bring. This implies that:

- Every effort must be made to guarantee and respect any residual capacity for autonomous decision, considering consent as an instrument through which the subject realizes his autonomy.
- The autonomy of the subject requires that all information be understood.
- The person's consent presupposes his/her ability to choose freely based on his preferences, moral values, life stages and circumstances.

First, it is necessary to inform the person with MCI, adapting the information to the cognitive abilities of the same, making every effort so that the patient can directly or indirectly communicate his preferences. The opinion of family members, for example, may be requested, but considered secondary to that of the patient.

The person with MCI who gave his/her informed consent to participate and is not comfortable during the sessions may at any time withdraw from the trial without any consequences.

In the specific case of the engAGE study, neither serious harmful effects on the person with MCI are foreseeable nor is there bad faith in the treatment proposal. The research teams proceed to ask the person with MCI to provide their informed consent to participate and strive to:

- ensure that he/she clearly understands the content of the information sheet and the consequences of his/her participation.
- create the best conditions in which he/her can ask questions and express his/her will.
- monitor throughout the course of the trial the persistence of his/her willingness to participate.

During the clinical interview, the contextual assessment of the ability to express an autonomous choice is carried out, assessing the presence of:

- Ability to express a choice.
- Ability to understand information relating to consent.
- Ability to give due weight to the situation and its possible consequences.
- Ability to use information rationally.

If this evaluation gives a positive result, informed consent is acquired from the person him/herself. Time and effort are devoted to providing correct and full information, the information sheets and the consent form is read together with the person with MCI and their caregiver, the opportunity to ask questions is given and the best conditions is created to decide. An additional opinion is requested from the main and reference caregiver on whether the person with MCI should participate in the project, what his/her wishes and feelings about participation may not have been expressed. If the subject then shows signs of dissent before and during each training session or shows behaviors that suggest that he/she is no longer willing to participate, the sessions are terminated, and the consent is automatically withdrawn.

Safety and security considerations

The hardware devices used are commercial devices and CE certified. The engAGE platform dashboards for older people and caregivers are loaded on a tablet held by the users.
Personal data collected during the trial is handled and stored in accordance with the General Data Protection Regulation (GDPR) [32]. All data and documentation related to the trial is stored in accordance with applicable regulatory requirements and access to data is restricted to authorized trial personnel. The project committed to the maintenance of participants' anonymity and confidentiality throughout all procedures, including screening, recruitment, testing, evaluation and dissemination procedures. Data collection, usage and storage procedures complied with national laws and the EU's GDPR [32] including the commitment of participants' the right to access, right to be informed, right to withdraw, and right to data erasure. Moreover, the servers are in the European Union and compliant to GDPR. Use of the study data is controlled by the principal investigator. Data collection is compliant with the principle of data minimization i.e. the collection of personal information from study participants is limited to what is directly relevant and necessary to accomplish the specific goals of the testing and evaluation work packages. Data entry is carried out using specific software, providing blocks and data entry checks, to reduce the number of entry errors. All screening data are discarded upon the project completion. During the testing procedures, all visual, auditory and sensory data that the robot collects and processes to function as planned are discarded after the procedures have been completed. The exception to this is the collection of the number of interactions that the robot logs with each participant. However, these interactions are anonymous. All research data shall be made openly available for secondary analysis 3 years after the project completion. The study findings are used for publication in peer-reviewed scientific journals and presentations in scientific meetings. Summaries of the results are also made available to investigators for dissemination within their clinics.
In the case of the engAGE project, a critical area of security is the servers (cloud or on-premises) where the solutions are deployed, or on which data are stored. These are provided with physical and logical protection. Also, the communication network architecture implements mechanisms of comprehensive network protection against intrusion such as Intrusion Prevention System, firewall and network antivirus filter. The core system is placed in a secure zone excluding the necessary communication modules located in the demilitarized zone, enabling data exchange with engAGE services, devices, and components. In the case of communication via an external network, strong mechanisms are required to guarantee the protection of transmitted data, their integrity, confidentiality and non-repudiation (e.g., TLS – Transport Layer Security). Authorization procedures are implemented specifying who is authorized to access the network and network services - access to services should be possible only for authorized users/devices by providing authentication and authorization mechanisms. Access to individual applications must require a user identifier and authentication (password, authentication certificate). The application functionality available to individual users is limited by the user's rights. The system architecture includes solutions that eliminate or significantly reduce the system's vulnerability to attacks as recommended in the Open Web Application Security Project (OWASP). Data is transferred using REST APIs using secured HTTPS protocol. In engAGE, different types of databases are used for storing data. These database servers give the option of encryption at several levels and provide flexibility in protecting data from disclosure (e.g. password storage encryption, data partition encryption, etc.).

Discussion

In a context such as the West and particularly Europe where dementia is a major societal challenge, researching and validating solutions that mitigate its impact on those directly or indirectly affected is of crucial importance. To date, there are countless technologies available as well as knowledge about interventions that provide benefit in combating cognitive decline in the elderly. However, just as

there are no effective drugs against MCI, there are no technological or non-technological interventions that-despite being promising-impact significantly on the problem. The proof of concept of the engAGE platform is therefore aimed at long-term testing of the integration of technological devices and services that have been shown to be promising by previous studies (such as social robotics, mobile apps, activity trackers, and ML algorithms), evaluating both their impact on the cognitive ability of elderly people with MCI but also on closely related aspects such as quality of life and sociality. In addition, the study strongly considers the importance of the usability and acceptability of the technology by the target group, being especially the elderly, as a key parameter to affirm its feasibility in future scenarios involving more countries and more participants. In addition to technological and clinical research, great emphasis is placed on ethics in this protocol, at a time in history when the use of artificial intelligence, robotics, and data protection are forcing us to carefully consider the impact of research on all the stakeholders, especially the most fragile ones.

Acknowledgements

This work was supported by a grant of the EU AAL Joint programme and Executive Agency for Higher Education, Research, Development and Innovation Funding (UEFISCDI) (RO), The Research Council of Norway (NO), Federal Department of Economic Affairs, Education and Research / State Secretariat for Education, Innosuisse (CH) and Italian Ministry of Health (IT) under the Consortium Agreement number aal-2021-8-159-CP.

Authors' contributions

GA led the writing of the manuscript; RB, EM, EF, and AM wrote the protocol; RB, EM, AM, GA, MB, FB, EF, and AB submitted the protocol in Italy; GA, EM, and AB registered the protocol on clinicaltrials.gov; LG and JG submitted the protocol in Switzerland; TG and RH submitted the submission of the protocol in Norway; AIM, TC and LTB contributed to the protocol as technical experts; IA is the engAGE project coordinator.

Conflicts of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Abbreviations

AAL: Ambient and Assisted Living
CG: Control Group
CH: Switzerland
EG: Experimental Group
EU: European Union
GDPR: General Data Protection Regulation
ICT: Information and Communication Technologies
IT: Italy
ML: Machine Learning
MCI: Mild Cognitive Impairment
NO: Norway

References

1. Osservatorio demenze dell'Istituto Superiore della Sanità. [Internet]. Available from: demenze.iss.it
2. National Dementia Strategy 2014–2019 [Internet]. Federal Office of Public Health (FOPH) and Swiss Conference of the Cantonal Ministers of Public Health (CMPH); 2018 [visited on 22nd April 2024]. Available from: https://www.bag.admin.ch/bag/en/home/strategie-und-politik/nationale-gesundheitsstrategien/demenz.html
3. Gjøra L, Strand BH, Bergh S, Borza T, Brækhus A, Engedal K, et al. Current and Future Prevalence Estimates of Mild Cognitive Impairment, Dementia, and Its Subtypes in a Population-Based Sample of People 70 Years and Older in Norway: The HUNT Study. Fink A. JAD. 2nd February 2021;79(3):1213–26.
4. Spector A, Thorgrimsen L, Woods B, Royan L, Davies S, Butterworth M, et al. Efficacy of an evidence-based cognitive stimulation therapy programme for people with dementia: Randomised controlled trial. Br J Psychiatry. September 2003;183(3):248–54.
5. Seitz DP, Brisbin S, Herrmann N, Rapoport MJ, Wilson K, Gill SS, et al. Efficacy and Feasibility of Nonpharmacological Interventions for Neuropsychiatric Symptoms of Dementia in Long Term Care: A Systematic Review. Journal of the American Medical Directors Association. July 2012;13(6):503-506.e2.
6. Bessey LJ, Walaszek A. Management of Behavioral and Psychological Symptoms of Dementia. Curr Psychiatry Rep. August 2019;21(8):66.
7. Woods B, Aguirre E, Spector AE, Orrell M. Cognitive stimulation to improve cognitive functioning in people with dementia. Cochrane Database Syst Rev. 15th February 2012; (2):CD005562.
8. Cavallo M, Hunter EM, Van Der Hiele K, Angilletta C. Computerized Structured Cognitive Training in Patients Affected by Early-Stage Alzheimer's Disease is Feasible and Effective: A Randomized Controlled Study. Arch Clin Neuropsychol. 6th September 2016;acn;acw072v1.
9. Bevilacqua R, Felici E, Cucchieri G, Amabili G, Margaritini A, Franceschetti C, et al. Results of the Italian RESILIEN-T Pilot Study: A Mobile Health Tool to Support Older People with Mild Cognitive Impairment. JCM. 22nd September 2023;12(19):6129.
10. Foster PP, Rosenblatt KP, Kuljiš RO. Exercise-Induced Cognitive Plasticity, Implications for Mild Cognitive Impairment and Alzheimer's Disease. Front Neur [Internet]. 2011 [visited on 22nd April 2024];2. Available from: http://journal.frontiersin.org/article/10.3389/fneur.2011.00028/abstract
11. Rajji TK. Impaired brain plasticity as a potential therapeutic target for treatment and prevention of dementia. Expert Opinion on Therapeutic Targets. 2nd January 2019;23(1):21–8.
12. Vitaliano PP, Zhang J, Scanlan JM. Is Caregiving Hazardous to One's Physical Health? A Meta-Analysis. Psychological Bulletin. November 2003;129(6):946–72.
13. AAL engAGE project, https://engage-aal-project.eu/
14. Anghel I, Cioara T, Salomie I, Rancea A, Bevilacqua R, Amabili G, et al. Cognitive decline management through theatre therapy, artificial intelligence, and social robots. In: 2023 IEEE 19th International Conference on Intelligent Computer Communication and Processing (ICCP) [Internet]. Cluj-Napoca, Romania: IEEE; 2023. p. 431–6. Available from: https://ieeexplore.ieee.org/document/10398682/
15. Antonesi G, Rancea A, Cioara T, Anghel I. Graph Learning and Deep Neural Network Ensemble for Supporting Cognitive Decline Assessment. Technologies. 24th December 2023;12(1):3.
16. The Global Deterioration Scale for assessment of primary degenerative dementia. AJP.

September 1982;139(9):1136–9.
17. Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool For Mild Cognitive Impairment. J American Geriatrics Society. April 2005;53(4):695–9.
18. Crook TH, Feher EP, Larrabee GJ. Assessment of Memory Complaint in Age-Associated Memory Impairment: The MAC-Q. Int Psychogeriatr. September 1992;4(2):165–76.
19. The Global Deterioration Scale for assessment of primary degenerative dementia. AJP. September 1982;139(9):1136–9.
20. Rockwood K. A global clinical measure of fitness and frailty in elderly people. Canadian Medical Association Journal. 30th August 2005;173(5):489–95.
21. Venkatesh, Thong, Xu. Consumer Acceptance and Use of Information Technology: Extending the Unified Theory of Acceptance and Use of Technology. MIS Quarterly. 2012;36(1):157.
22. Russell D, Peplau LA, Cutrona CE. The revised UCLA Loneliness Scale: Concurrent and discriminant validity evidence. Journal of Personality and Social Psychology. September 1980;39(3):472–80.
23. Zarit SH, Todd PA, Zarit JM. Subjective Burden of Husbands and Wives as Caregivers: A Longitudinal Study. The Gerontologist. 1st June 1986;26(3):260–6.
24. Tennant R, Hiller L, Fishwick R, Platt S, Joseph S, Weich S, et al. The Warwick-Edinburgh Mental Well-being Scale (WEMWBS): development and UK validation. Health Qual Life Outcomes. dicembre 2007;5(1):63.
25. Rabin R, Charro FD. EQ-SD: a measure of health status from the EuroQol Group. Annals of Medicine. January 2001;33(5):337–43.
26. Thorgrimsen L, Selwood A, Spector A, Royan L, De Madariaga Lopez M, Woods RT, et al. Whose Quality of Life Is It Anyway?: The Validity and Reliability of the Quality of Life-Alzheimer's Disease (QoL-AD) Scale. Alzheimer Disease & Associated Disorders. October 2003;17(4):201–8.
27. Bangor A, Kortum PT, Miller JT. An Empirical Evaluation of the System Usability Scale. International Journal of Human-Computer Interaction. 29th July 2008;24(6):574–94.
28. World Medical Association Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. JAMA. 27th November 2013;310(20):2191.
29. EU guidelines on ethics in artificial intelligence: Context and implementation, European Parliament, 2019, Available from: https://www.europarl.europa.eu/thinktank/en/document/EPRS_BRI(2019)640163
30. Battistuzzi L, Sgorbissa A, Papadopoulos C, Papadopoulos I, Koulouglioti C. Embedding Ethics in the Design of Culturally Competent Socially Assistive Robots. In: 2018 IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS) [Internet]. Madrid: IEEE; 2018. p. 1996–2001. Available from: https://ieeexplore.ieee.org/document/8594361/
31. Sviluppi della robotica e della roboetica, Presidency of Italian Ministers Council, 2017, Available from: http://www.sossanita.it/doc/2017_08_robotica-cnb.pdf
32. European Commission. Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation) (Text with EEA relevance) [Internet]. European Commission; 2016. Available from: https://eur-lex.europa.eu/eli/reg/2016/679/oj

Supplementary Files

Multimedia Appendixes

Proposal accepted by AAL Programme funded by European Union.
URL: http://asset.jmir.pub/assets/d42d3844ea7988e549f5b0d70aec4d99.pdf