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Improvement of cognitive and psychological long-COVID symptoms through tablet-based training

Submission date
05/01/2025

Recruitment status
No longer recruiting

Registration date
07/01/2025

Overall study status
Completed

Last Edited
22/01/2025

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims:
Post-COVID-19 condition (PCC) (long COVID) is a complex disease with a variety of symptoms causing individual challenges and high economic burden. Cognitive impairment and psychological complaints are among the most common consequences for patients suffering from PCC. Given the limited cognitive training options available to date, this study examined a 3-month tablet-based training program, tailored for individuals with PCC, addressing the cognitive and psychological symptoms.

Who can participate?
Patients aged 18 years and over suffering from cognitive and psychological long-COVID symptoms

What does the study involve?
The study involved two groups (intervention group, control group) and three measurement timepoints (baseline, follow-up 1 after 3 months, and follow-up 2 after 6 months). The intervention group received a 3-month tablet-based training program, conducted from home, involving cognitive, physiotherapy, and relaxation exercises. Both groups underwent a thorough neuropsychological assessment (assessed domains: attention, memory, executive functions, word fluency, subjective cognitive complaints, fatigue, depression, anxiety, and quality of life) before the training, after 3 months of training, and at 6 months to assess long-term effects. The researchers further conducted exploratory analyses to examine the relationship between the number of post-COVID symptoms and cognition, as well as the impact of disease duration on this relationship.

What are the possible benefits and risks of participating?
Possible benefits included improvements in cognitive functions (e.g., memory, attention, executive function) and/or mitigation of adverse psychological symptoms (e.g., depression, anxiety). No risks or harms were reported.

Where is the study run from?
Medical University of Graz (Austria)

When is the study starting and how long is it expected to run for?
October 2021 to December 2023

Who is funding the study?
Austrian Research Promotion Agency (FFG, project number: FO999887709)

Who is the main contact?
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
A tablet-based intervention study to alleviate cognitive and psychological symptoms in patients with post-COVID-19 condition: a randomized controlled trial

Study objectives
It is hypothesized that participation in our training program alleviates cognitive and psychological symptoms associated with post-COVID-19 condition (PCC) in various domains such as memory, attention, and executive function. In addition, the study examined the efficacy of the training in reducing subjective cognitive complaints, fatigue and negative emotions such as anxiety or depression, and attempted to increase the quality of life of those affected by PCC. In a set of exploratory analyses, the researchers were further interested in the association between post-COVID symptom count and cognition, and the impact of disease duration on this correlation.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 01/02/2022, Ethics committee of the Medical University of Graz (Neue Stiftingtalstraße 6 - West, Q 04, Graz, 8010, Austria; +43 (0)316 385 71400; ethikkommission@medunigraz.at), ref: 34-206 ex 21/22 1012-2022

Study design
Single-centre randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Home, Hospital

Study type(s)
Treatment, Efficacy

Participant information sheet
See study outputs table

Health condition(s) or problem(s) studied
Long-COVID/post-COVID-19-condition

Interventions
Patients with self-reported symptoms of PCC (i.e., persistent symptoms or newly emerged symptoms after the resolution of an acute COVID-19 infection) were invited to undergo a comprehensive neuropsychological assessment as well as structural and functional MRI at the Medical University of Graz, Austria between October 2022 and November 2023. Due to significant impairment (high post-COVID-19 functional status combined with high levels of fatigue), two individuals were excluded from further study participation although initially meeting inclusion criteria (after extensive discussion, these individuals were deemed unable to adequately complete the training over the 3-month duration). The remaining 40 participants were randomly (block randomization, block size = 6) assigned to either an intervention (n = 20) or a wait-list control group (n = 20) by MK after completing a baseline (BL) testing. The person who conducted the cognitive assessment (ML) did not know to which of the two groups a patient was assigned after testing. Individuals assigned to the intervention group received a free tablet-based training program and had three on-site neuropsychological examinations with three months between each examination period to assess both a post-training effect (BL-follow up 1 [FU1]) as well as the stability of this effect (FU1-FU2). Those who were assigned to the control group received no training or treatment as usual (since no validated treatment existed at the time the study was conducted) for the first three assessments (BL-FU1-FU2) but they received the same training after a 6-month waiting period in order to assess their post-training effect (FU2-FU3) as well. In the end, both groups were combined to assess pre-post effects in a larger sample.

Before the long-COVID patients allocated to the intervention group were provided with the tablet and the installed training, each received individual on-site instruction, during which all participants became familiar with the technology and the exercises. The handling of the exercises was relatively simple and required no specific technical knowledge. Therefore, also older participants had no difficulty using the training program, as it was ensured beforehand that they felt comfortable with using the tablet. The intervention combined relaxation exercises (Jacobson muscle relaxation), physiotherapy exercises and cognitive training. As the training was conducted asynchronously and from home, we were able to offer a location-independent training program, allowing patients to train as often as they wanted and at flexible times. The cognitive part included tasks such as remembering and recalling sequences (visual memory; e.g., remembering a sequence of fields and then clicking them in the same order), attention/reaction time exercises (e.g., participants had to click on the screen as fast as possible whenever they saw a number appear anywhere on it, thereby training their sustained attention over an extended period), calculation tasks (e.g., solving mathematical calculation tasks), exercises to train executive functions (e.g., exercises with inhibition tasks), as well as playful activities such as the game “memory” or quiz tasks (to train short- and long-term memory). It was recommended to train at least three times a week for at least 30 minutes each session, with more frequent training being encouraged. Additionally, various difficulty levels were implemented to adapt the tasks to the cognitive abilities of the participants. Patients were contacted by phone every two weeks to ensure they continued training and to receive feedback. They could contact the study authors at any time if problems occurred.

Intervention Type
Device

Pharmaceutical study type(s)

Not Applicable

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
-

Primary outcome measure
1. Global cognitive impairment measured using the Montreal Cognitive Assessment (MoCA) (questionnaire) at BL, FU1 and FU2.
Attention assessed using the 'Digit Span Forward' and 'Digit Span Backward' task from the German version of the Neuropsychological Assessment Battery (NAB), as well as the Trail Making Test A (TMT-A) at BL, FU1 and FU2
2. Executive function measured using the subtests 'Planning' and 'Categories' from the Neuropsychological Assessment Battery (NAB) as well as the Trail-Making-Test B (TMT-B) at BL, FU1 and FU2
3. Memory assessed using the subtest 'Word List Learning' from the Neuropsychological Assessment Battery (NAB) at BL, FU1, and FU2.
4. Word fluency measured using the Regensburger Word Fluency Test (RWT) with both the formal-lexical and semantic subtests at BL, FU1, and FU2
5. Subjective cognitive complaints assessed using a translated version of the Questionnaire de Plainte Cognitive at BL, FU1 and FU2.
6. Fatigue measured using the German version of the Fatigue Impact Scale (FIS-D) at BL, FU1 and FU2
7. Depression and anxiety assessed using the General Depression Scale (ADS) and the Hospital Anxiety and Depression Scale (HADS-A and HADS-D) at BL, FU1 and FU2
8. Quality of life measured using the German version of the WHOQoL-BREF (World Health Organization Quality of Life) in its short form at BL, FU1 and FU2

Secondary outcome measures
1. The number of symptoms during the acute COVID-19 illness was assessed via self-report only at Baseline (BL) only. The patients were asked to select from a list of 64 symptoms those that applied to them during their acute illness.
2. The number of long-COVID symptoms was assessed via self-report at BL, FU1 and FU2. The patients were asked to select from a list of 64 symptoms those that applied to them during the respective timepoint.
3. The long-COVID disease duration was assessed via self-report at Baseline (BL) only. The patients stated the time of their COVID-19 diagnosis and subsequently since how many weeks /months they suffered from long-COVID.

Overall study start date
01/10/2021

Completion date
31/12/2023

Eligibility

Key inclusion criteria

1. Ongoing or newly developed symptoms 3 months after a positive COVID-19 infection
2. Symptoms lasting for at least 2 months with no other explanation
3. Symptoms leading to a new health impairment (self-report)
4. Deterioration of a pre-existing disease (self-report)
5. None of the following pre-existing diseases: dementia, multiple sclerosis, Parkinson’s disease, stroke
6. No participation on any other pharmacological or psychological training study aiming to improve cognitive or psychological complaints

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Upper age limit
100 Years

Sex
Both

Target number of participants
28

Total final enrolment
40

Key exclusion criteria
In general, patients were only excluded if they did not meet the inclusion criteria. However, due to significant impairment (high post-COVID-19 functional status combined with high levels of fatigue), two individuals were excluded from further study participation although initially meeting inclusion criteria (after extensive discussion, these individuals were deemed unable to adequately complete the training over the 3-month duration).

Date of first enrolment
01/10/2022

Date of final enrolment
09/11/2023

Locations

Countries of recruitment
Austria

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ROR
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Funder(s)

Funder type
Government

Funder Name
Österreichische Forschungsförderungsgesellschaft

Alternative Name(s)
Austrian Research Promotion Agency, The FFG, The Österreichische Forschungsförderungsgesellschaft mbH (FFG), Die Österreichische Forschungsförderungsgesellschaft, Österreichische Forschungsförderungsgesellschaft mbH, FFG – Austria, FFG

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Austria

Results and Publications

Publication and dissemination plan
Currently the manuscript is submitted to the Journal of Medical Internet Research

Intention to publish date
14/06/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Marisa Koini (marisa.koini@medunigraz.at) or Manuel Leitner (manuel.leitner@medunigraz.at)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			07/01/2025	No	Yes
Basic results		22/01/2025	22/01/2025	No	No