Neuroinflammation and post-infectious fatigue in individuals with and without Covid-19

Published: 01-07-2021
Last updated: 17-01-2025

The aim of this study is to quantify neuroinflammation and whole-body inflammation with [18F]DPA-714 PET scans in post-COVID-19 patients and relate it to cognitive, psychiatric and post-infectious fatigue symptoms.

Ethical review	Approved WMO
Status	Completed
Health condition type	Central nervous system infections and inflammations
Study type	Observational invasive

Summary

ID

NL-OMON54244

Source
ToetsingOnline

Brief title
COVFATI

Condition

- Central nervous system infections and inflammations

Synonym
corona

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum
Source(s) of monetary or material Support: ME/CVS stichting

Intervention

Keyword: covid-19, neuroinflammation, PET

Outcome measures

Primary outcome

The primary parameter is the measurement of neuro-inflammation in vivo with the [18F]DPA-714 (±286MBq, 4,9mSv) 70 minutes PET scan, alternately capturing brain (60 minutes) and body (10 minutes; pelvic to head) with both continuous on-line and manual arterial blood sampling for full quantification ([18F]DPA-714 volume of distribution).15,16. Brain MRI will be performed for functional and anatomical information.

Secondary outcome

Secondary parameters include whole-body inflammation as measured with 60-70 min body PET. In adddition, we will use CIS, BDI, GAD7 and neuropsychological evaluation to assess chronic fatigue, depressive, anxiety and cognitive symptoms, partially for descriptive purposes. In addition, questionnaires to evaluate smell and taste complaints will be evaluated.

Study description

Background summary

The scale of the current COVID-19 pandemic is unprecedented with >500000 infections to date in the Netherlands and >54 million globally (https://COVID19.who.int). Already a great number of post-COVID-19 patients have developed *chronic* complaints, such as fatigue and cognitive complaints, which persists >2months after infection (36-53%).1,2 Post-infectious fatigue (PIF) is a condition characterized by chronic, debilitating, and unexplained fatigue3, months after an infection.45-7 There is evidence that peripheral8-12 and neuroinflammation13,14 are involved in post-infectious fatigue and

cognitive complaints, but precise pathophysiological mechanisms and causal relationship with viral infections are still unknown.

Study objective

The aim of this study is to quantify neuroinflammation and whole-body inflammation with [18F]DPA-714 PET scans in post-COVID-19 patients and relate it to cognitive, psychiatric and post-infectious fatigue symptoms.

Study design

Cross-sectional observational case-control study

Study burden and risks

[18F]DPA-714 is a tracer with excellent in vivo stability and biodistribution. It has been used as a tracer in animal and human studies in multiple neurological diseases, including multiple sclerosis (MS), Alzheimer*s disease (AD) and post-stroke, all of which did not identify AEs or SAEs. Furthermore, [18F]DPA-714 gives relatively minor radiation exposure, similar to other fluorine-labeled tracers, within guidelines for radiation exposure for healthy controls. Finally, withdrawal of arterial blood poses a very minor risk of complications, such as infection at the injection site. There is no increased risk associated with any of the other examinations performed (neuropsychological or psychiatric evaluation or MRI), but these may be experienced as burdensome by certain individuals. No patient-specific benefits are expected. We expect TSPO specific binding to be increased in COVID-19 patients as compared to controls and post-COVID-19 individuals without chronic fatigue or cognitive complaints.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Group 1. In order to participate in this study, individuals with a previous COVID-19 infection and with post-infectious fatigue or cognitive complaints should meet the following criteria:
1) The patient was diagnosed with symptomatic COVID-19, confirmed by a positive PCR for SARS-CoV-2, positive SARS-CoV-2 serology or CO-RADS (COVID-19 Reporting and Data System) 4 or 5 on CT-scan, or antigen quicktest, or had typical symptoms and was part of a household in which another person was tested positive by PCR 2 weeks before or after the first day of illness;
2) The patient is 3 months after being diagnosed with COVID-19 or after hospital discharge in case the patient was admitted.
3) The patient experiences severe levels of fatigue (>= 40) on the fatigue subscale of the Checklist Individual Strength [CIS-fatigue]) and/or cognitive complaints (>= 15) on the concentration subscale of the Checklist Individual Strength [CIS-concentration]. The severe fatigue or cognitive complaints started with or increased substantially directly after the onset of symptoms of COVID-19
4) The patient reports physical/social disability (<= 65 on the Rand36 physical functioning subscale or a score of >= 10 on the Work and Social Adjustment Scale [WSAS]10;
5) The patient is in the range 30-65 years of age (to ensure radiation safety)
6) The patient has sufficient command of the Dutch language
7) Genotyping of rs6971 must show that patient is a mixed or high affinity binder

Group 2. In order to participate in this study, individuals with a previous COVID-19 infection and without post-infectious fatigue or cognitive complaints should meet the following criteria:
1) The patient was diagnosed with symptomatic COVID-19, confirmed by a positive PCR for SARS-CoV-2, positive SARS-CoV-2 serology or CO-RADS 4 or 5 on CT-scan,

or antigen quicktest, or had typical symptoms and was part of a household in which another person was tested positive by PCR 2 weeks before or after the first day of illness;
2) The patient is 3 months after being diagnosed with COVID-19 or after hospital discharge in case the patient was admitted.
3) The patient experiences no significant levels of fatigue (< 35 on the fatigue subscale of the Checklist Individual Strength [CIS-fatigue]) or cognitive complaints (<15 on the concentration subscale of the Checklist Individual Strength [CIS-concentration]) and does not subjectively major symptoms of fatigue. or cognitive complaints. Based upon average of normal population +1SD
4) The patient reports no physical/social disability (> 65 on the Rand36 physical functioning subscale or a score of < 10 on the Work and Social Adjustment Scale [WSAS]10;
5) The patient is in the range 30-65 years of age (to ensure radiation safety)
6) The patient has sufficient command of the Dutch language
7) Genotyping of rs6971 must show that patient is a mixed or high affinity binder

Group 3. Healthy controls should meet the following criteria:
1) Should be negatively tested for COVID-19 trough PCR, serology, antibodies, or via antigen quicktest
2) No evidence for substantial fatigue or cognitive complaints as evidenced by the CIS subscale fatigue (<35) and CIS subscale concentration (<15) and does not subjectively major symptoms of fatigue or cognitive complaints. Based upon average of normal population +1SD
3) The patient is in the range 30-65 years of age (to ensure radiation safety)
4) The patient has sufficient command of the Dutch language
5) Genotyping of rs6971 must show that patient is a mixed or high affinity binder

Exclusion criteria

1) Rs6971 shows low affinity binding
2) Patients who are unable to lay still for scanning due to claustrophobia or severe back pain or trypanophobia (fear of needles)
3) Gross neurological pathology (strategic or lobar infarcts) on MRI or CT that may interfere with the interpretation of the PET scan.
4) Post-infectious complaints before COVID-19 or any other current disease of infection that is known to cause substantial fatigue

Study design

Design

Study phase:	2
Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	03-02-2022
Enrollment:	85
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[18F]DPA-714
Generic name:	[18F]DPA-714

Ethics review

Approved WMO Date:	01-07-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-12-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-04-2022
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-08-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-11-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-03-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2021-000781-15-NL
CCMO	NL77033.029.21