TSPO PET tracing In patients with and without Cognitive impairment in the long-term after AneurySmal Subarachnoid haemorrhage

Published: 06-11-2019
Last updated: 09-04-2024

To determine whether reactive gliosis persists >3 years after SAH and whether this response relates to cognitive impairment after SAH.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Central nervous system vascular disorders
Study type	Observational invasive

Summary

ID

NL-OMON55660

Source
ToetsingOnline

Brief title
PICASSO

Condition

- Central nervous system vascular disorders
- Cognitive and attention disorders and disturbances
- Aneurysms and artery dissections

Synonym
aneurysmal subarachnoid hemorrhage (aSAH), bleeding between the coverings of the brain due to an aneurysm

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Cognition, Neuroinflammation, Subarachnoid hemorrhage, TSPO

Outcome measures

Primary outcome

All subjects will undergo neuropsychological testing on 5 cognitive domains, and crude test scores will be transformed into z-scores based on scores of a matched control group. . Outcomes will be dichotomized into cognitive impaired or not-cognitive impaired. Furthermore, each subject will be asked to fill out 3 questionnaires to evaluate self-reported cognitive complaints. After this, patients will proceed to undergo 3Tesla brain MRI and 60 minute dynamic Positron Emission Tomography (PET) scanning using a [18F]DPA-714 ligand, where a simplified reference tissue model (SRTM) will be used in quantitation with cerebellar gray matter as pseudo-reference area. Using this method, tracer binding potential (BPND) will be obtained as an estimator of distribution volume ratio (DVR) and differences in BPND between subgroups. It will be investigated if tracer binding potential is correlated with cognitive impairment.

Differences in TSPO binding capacity between 3 groups:

- Patients with cognitive impairment at least 3 years after aSAH

- Patients without cognitive impairment at least 3 years after SAH

- Controls with unruptured intracranial aneurysms

Secondary outcome

- Domain and severity of cognitive impairment after SAH

- Results of questionnaires

- Demographic variables (as listed in paragraph 6.3. Study procedures)

- SAH characteristics (as listed in paragraph 6.3. Study procedures).

Study description

Background summary

Long-term cognitive impairment occurs in 30% of patients surviving aneurysmal subarachnoid haemorrhage (SAH). Recent insights show that this impairment might be due to loss of synapses or impaired synaptic function, caused by an inflammatory response to injury known as reactive gliosis.

Study objective

To determine whether reactive gliosis persists >3 years after SAH and whether this response relates to cognitive impairment after SAH.

Study design

Cross-sectional cohort study

Study burden and risks

No patient-specific benefits will be reached in this study. However, this study has the group benefit of gaining insight in the (patho)physiology of these cognitive impairment, while identifying potential treatment opportunities. Risks associated with participation are very low to negligible: in radio ligand injection there is a minor risk of infection. Furthermore, MRI scanning poses minor known risks associated with the magnetic field, which we will address by carefully screening subjects beforehand. [18F]DPA-714 PET-scanning has no reported AEs or SAEs in prior research and radiation exposure has been shown to be similar to other fluoride-labeled ligands, which is well under the threshold as established by the European Association of Nuclear Medicine (EANM).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Subjects (n = 14) with aSAH >3 years ago and cognitive impairment
- Admitted to the UMCU with aneurysmal SAH at least 3 years ago, defined as
o Blood on initial non-contrast CT or bilirubin in cerebrospinal fluid (CSF)
o A proven aneurysm, demonstrated by computed tomography angiography (CTA), digital subtraction angiography (DSA) or magnetic resonance angiography (MRA)
- Genotyping of rs6971 must show that patient is a high affinity binder
- Functional independence (defined as modified rankin scale (mRS) or 0-2)
o mRS (Dutch) table can be found in Appendix 1
- Patient must have been at least 18 years of age at time of visit to the outpatient clinic.
- Neuropsychological evaluation shows cognitive impairment.

Subjects (n = 14) with aSAH >3 years ago and no cognitive impairment
- Admitted to the UMCU with aneurysmal SAH at least 3 years ago, defined as
o Blood on initial non-contrast CT or bilirubin in CSF
o A proven aneurysm, demonstrated by CTA, DSA or MRA
- Genotyping of rs6971 must show that patient is a high affinity binder
- Functional independence (defined as mRS or 0-2)
o mRS (Dutch) table can be found in Appendix 1
- Patient must have been at least 18 years of age at time of visit to the outpatient clinic.
- Neuropsychological evaluation shows no cognitive impairment.

Controls (n = 8) with unruptured aneurysms
- Admitted to the UMCU with an unruptured aneurysm, defined as
o A proven aneurysm, demonstrated by CTA, DSA or MRA
- Genotyping of rs6971 must show that patient is a high affinity binder
- Functional independence (defined as mRS of 0-2)
- Patient must have been at least 18 years of age at time of visit to the outpatient clinic.
- Neuropsychological evaluation shows no cognitive impairment.

Exclusion criteria

- Contra-indication for PET-MRI scanning (such as severe lower back pain or claustrophobia)
- Pregnancy
- Exposure to ionic radiation (clinical or experimental) in the past year

Study design

Design

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:	Recruitment stopped
Start date (anticipated):	23-11-2020
Enrollment:	36
Type:	Actual

Ethics review

Approved WMO Date:	06-11-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	30-01-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-07-2021
Application type:	Amendment
Review commission:	METC NedMec

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
CCMO	NL69428.041.19