Multiomics in systemic inflammation driven brain aging in humans

Published: 12-08-2024
Last updated: 27-12-2024

Using single-cell transcriptomic and epigenetic profiles of (immune) cells in liquor to investigate which biological and cellular processes are involved in (accelerated) brain aging and cognitive decline after systemic inflammation.

Ethical review	Approved WMO
Status	Pending
Health condition type	Encephalopathies
Study type	Observational invasive

Summary

ID

NL-OMON56946

Source
ToetsingOnline

Brief title
UNCOVERS

Condition

- Encephalopathies
- Vascular therapeutic procedures
- Aneurysms and artery dissections

Synonym
postoperative cerebral dysfunction, Postoperative cognitive decline (POCD)

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Brain aging, Neuroinflammation, Single-cell omics, Thoracic-abdominal aortic aneurysm (TAAA)

Outcome measures

Primary outcome

Primary endpoint are biological pathways and markers based on transcriptomic

and epigenetic data, with patients divided into two groups based on cognitive

assessment after 6 months.

Secondary outcome

Primary endpoint are biological pathways and markers based on transcriptomic

and epigenetic data, with patients divided into two groups based on cognitive

assessment after 12 months.

Study description

Background summary

Systemic inflammation activates immune cells in the brain and causes neuroinflammation, which is believed to play a key role in the development of cognitive decline due to post-systemic inflammation. Major cardiovascular surgery causes a severe systemic inflammatory response. Systemic inflammation-induced neuroinflammation is believed to be a major cause of postoperative cognitive decline (POCD) in patients who have undergone major surgery, such as thoracic aortic aneurysm (TAA) repair surgery.

Study objective

Using single-cell transcriptomic and epigenetic profiles of (immune) cells in liquor to investigate which biological and cellular processes are involved in (accelerated) brain aging and cognitive decline after systemic inflammation.

Study design

Time series design observational study.

Study burden and risks

- Blood and cerebrospinal fluid sampling occurs through intravascular catheters and the external lumbar drain that are already present due to the standard of care related to the surgery. Therefore, this does not add an additional burden.
- Patients will undergo three brain MRIs (pre-, within 2 weeks post-surgery during their hospitalization once they are sufficiently restored from the surgery, and at 6 months visit to outpatient clinic). The MRI bears some burden but with a low to negligible risk.
- Patient will undergo a total of 4 neuropsychological assessments. These will be either during the hospital stay (first two), during their clinical routine visit to the outpatient clinic at the hospital (6 months) and at their own house (12 months). These bear little burden and a low to negligible risk.

Contacts

Public
Radboud Universitair Medisch Centrum

Geert Grooteplein-Zuid 10
Nijmegen 6525GA
NL
Scientific
Radboud Universitair Medisch Centrum

Geert Grooteplein-Zuid 10
Nijmegen 6525GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Planned for elective thoraco-abdominal aortic aneurysm repair that also have an ELD as part of their routine clinical care at Radboudumc

Exclusion criteria

- Disease states associated with a state of neuroinflammation: brain or spinal surgery within the last 6 months, meningitis or brain infection within the last 6 months, presence of a CSF catheter or shunt, presence of known brain tumor, brain injury (e.g., stroke, or subarachnoid hemorrhage) within the last 12 months, moderate-severe brain trauma in previous medical history, chronic active alcoholism or substance use.
- Pre-existing dementia or neurodegenerative disease
- Cognitive impairment interfering with the ability to understand informational study material.
- Chronic (>2 weeks) use of immunosuppressive agents (see table 3.3.A, below)
- Concomitant diseases resulting in severe immunosuppression (e.g., HIV, hematological malignancies)
- Patients that do not speak Dutch or analphabetic patients.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2024
Enrollment:	0
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	12-08-2024
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL86164.091.24