Blood-brain barrier in cerebral small vessel disease.

No registrations found.

Ethical review	Positive opinion
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON26559

Source
Nationaal Trial Register

Health condition

Blood-brain barrier, cerebral small vessel disease, lacunar stroke, cognitive impairment, DCE-MRI

Sponsors and support

Primary sponsor: Maastricht University Medical Center
Source(s) of monetary or material Support: Nederlandse Organisatie voor Wetenschappelijk Onderzoek (NWO)
(= Netherlands Organisation for Scientific Research)

Intervention

Outcome measures

Primary outcome

1. Quantified BBB permeability in cSVD patients and healthy controls;

2. Cognitive function, related to BBB permeability, at baseline and at follow-up.

Secondary outcome

Structural brain lesions on MRI, related to BBB permeability, at baseline and at follow-up.

Study description

Background summary

Cerebral small vessel disease (cSVD) is a disorder involving the small brain arteries. It is associated with structural lesions on brain MRI such as white matter lesions (WML), lacunar infarcts and brain microbleeds. Clinically, cSVD is associated with lacunar stroke (LACI) and vascular cognitive impairment (VCI).

Recent, preliminary studies showed that dysfunction and leakage of the blood-brain barrier (BBB), a neuro-vascular unit in the brain with protective properties, may play a major role in the pathophysiology of cSVD. However, up till now only limited qualitative data are available on the role of BBB permeability in cSVD.

The study objectives are 1. to quantify the BBB permeability using dynamic contrast-enhanced MRI in cSVD patients, in comparison to healthy control subjects, 2. to determine the relationship between BBB permeability and the extent of WML, and 3. to examine the relationship between BBB permeability and cognitive function.

It will be a prospective, observational cohort study. Over a period of 2 years we will include two patient groups with clinical cSVD, namely 40 LACI patients and 40 VCI patients, and 40 healthy controls . All participants will undergo a standard brain MRI to determine the extent of WML, a dynamic contrast-enhanced MRI to quantify BBB permeability and a neuropsychological assessment to determine cognitive function. The acquired data will be subjected to statistical analysis and the relationship between BBB permeability, WML and cognition in cerebral small vessel disease, will be determined.

Study objective

1. Blood-brain barrier permeability is quantitively increased in patients with cerebral small vessel disease compared to healthy controls;

2. Blood-brain barrier permeability is associated with cognitive function in patients with cerebral small vessel disease;

3. Blood-brain barrier permeability can predict future cognitive decline in patients with cerebral small vessel disease.

Study design

Data will be gathered at baseline (t=0), and after two years (t=2).

Intervention

Participants will receive:

At baseline:

1. A structural brain MRI scan;

2. A DCE-MRI scan;

3. A neuropsychological assessment;

4. Blood sampling;

5. Sublingual glycocalyx measurement.

At follow-up:

1. A 2nd structural brain MRI;

2. A 2nd neuropsychological assessment.

Contacts

Public
P. Debyelaan 25
C.E. Zhang
Maastricht 6229 HX
The Netherlands
+31 (0)43 3872907
Scientific
P. Debyelaan 25
C.E. Zhang
Maastricht 6229 HX
The Netherlands

+31 (0)43 3872907

Eligibility criteria

Inclusion criteria

Patients with lacunar stroke, patients with mild vascular cognitive impairment (VCI), and healthy subjects will be included.

Criteria for all subjects:

1. Age >18 year.

Criteria specifically for lacunar stroke patients:

1. A first-ever acute lacunar stroke.

Criteria specificaly for mild VCI due to cerebral small vessel disease (cSVD):

1. Subjective complaints of cognitive functioning and objective cognitive impairment in at least 1 cognitive domain on cognitive testing, and;

2. A Clinical Dementia Rating ≤1 and a MMSE ≥20 (i.e. no dementia), and;

3. Vascular lesions on brain MRI (lacunar infarts, white matter lesions, deep microbleeds) that suggest a link between the cognitive deficit and cSVD.

Healthy control subjects:

1. Healthy control subjects included from the general and matched to the LACI and mild VCI patients according to gender and age.

Exclusion criteria

Exclusion criteria for all subjects:

1. Age <18 year;

2. Cerebrovascular abnormalities in history:

A. Ischemic stroke;

B. Haemorrhagic stroke (subarachnoid or intracerebral).

3. Contra indications for MRI/DCE-MRI:

A. Heart valve prosthesis;

B. Pacemaker;

C. Intracerebral clips (aneurysm);

D. Intra-ocular metal pieces;

E. Cochlear implant;

F. Claustrophobia;

G. Poor kidney function (GFR<30ml/min);

H. Previous allergic reaction to contrast agent (gadobutrol).

4. Psychiatric disorders associated with (temporarily) cognitive decline (e.g. depression, psychosis).

Group specific exclusion criteria:

Lacunar stroke:

1. Potential cardiac embolic source (e.g. atrial fibrillation);

2. Stenosis of ≥50% of one or both internal carotid arteries.

Mild VCI due to cSVD:

1. Clinical and/or subclinical cortical events;

2. Other causes for cognitive impairment (e.g. Alzheimers Disease).

Healthy subjects:

1. Clinically overt cardiovascular diseases;

2. Clinically overt cerebrovascular diseases;

3. Disease of the central nervous system (e.g. Multiple Sclerosis, brain tumor/metastasis);

4. Extensive structural lesions on MRI associated with cSVD;

5. Cognitive impairment (i.e. objective and/or subjective cognitive deficits).

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non-randomized controlled trial
Masking:	Single blinded (masking used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2013
Enrollment:	120
Type:	Anticipated

Ethics review

Positive opinion

Date:	09-01-2013

Application type: First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 41443
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL3620
NTR-old	NTR3786
CCMO	NL41952.068.12
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON41443

Study results

Summary results
N/A