Blood-brain barrier in cerebral small vessel disease.

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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...

Ethische beoordeling	Positief advies
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON26559

Bron
Nationaal Trial Register

Aandoening

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

Ondersteuning

Primaire sponsor: Maastricht University Medical Center
Overige ondersteuning: Nederlandse Organisatie voor Wetenschappelijk Onderzoek (NWO) (= Netherlands Organisation for Scientific Research)

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

1. Quantified BBB permeability in cSVD patients and healthy controls;
2. Cognitive function, related to BBB permeability, at baseline and at follow-up.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksopzet

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

Onderzoeksproduct en/of interventie

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.

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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).

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	Niet-gerandomiseerd
Blindering:	Enkelblind
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-03-2013
Aantal proefpersonen:	120
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	09-01-2013

Soort: Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 41443
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten

Samenvatting resultaten
N/A