Midlife hypertension and structural and functional brain MRI: catching the first signs of cerebral small vessel disease

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Primary objectives:1. Examine abnormalities in brain (micro)structure and vascular function in patients with hypertension aged 18-40 2. Determine the effects of blood pressure increase and subsequent blood pressure reduction during a period of...

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

Summary

ID

NL-OMON51980

Source
ToetsingOnline

Brief title
HYPERINTENSE

Condition

- Central nervous system vascular disorders
- Vascular hypertensive disorders

Synonym
Hypertension, increased blood pressure

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: Cerebrovascular disease, Hypertension, Magnetic resonance imaging, Midlife

Outcome measures

Primary outcome

Neuroimaging markers of SVD

Secondary outcome

Measures of cognitive and motor functioning (using standardised tests and

questionnaires), circulating markers of inflammation

Study description

Background summary

Cerebral small vessel disease (SVD) describes a set of pathologies affecting the smallest blood vessels in the brain. SVD contributes to up to a fifth of ischemic and hemorrhagic strokes en is the main vascular cause of dementia. On MRI, SVD is marked by different types of lesions, including white matter abnormalities, and small infarcts and hemorrhages. Recent studies indicate that SVD develops slowly over the years, starting presumably decades before the typical MRI lesions become apparent. High blood pressure plays an important role in the development of SVD MRI lesions. However, it remains unclear exactly how hypertension leads to vascular pathology. To gain more insight into how hypertension leads to SVD it is important to study mechanisms in individuals (largely) free of SVD, that is before midlife.

Study 1: Cross-sectional

To examine if there are cerebral abnormalities present following hypertension before MRI markers of SVD have manifested, we will do high-resolution 3T MRI in 100 young (18-40 years) hypertensive adults. In addition to MRI, during each visit patients will undergo standardised tests and questionnaires to probe cognitive and motor functioning, and lifestyle and medical information. We will compare this group to normotensive, healthy age-matched participants of the Healthy Brain Study to examine if there are abnormalities following high blood pressure.

Study 2: Longitudinal

The prevalence of hypertension in the Netherlands in adults aged 30-49 years is approximately 10-20%. Part of the patients with hypertension are referred to an internist to identify the cause(s) of the hypertension. As part of the routine diagnostic work up, antihypertensive agents are temporarily withdrawn. As a consequence blood pressure will increase, followed by a decrease in blood pressure once antihypertensive agents are restarted. This period of medication withdrawal and subsequent restart offers a unique opportunity to study within subjects the acute effects of blood pressure increase and subsequent decrease on several MRI measures of SVD. In HYPERINTENSE 100 patients with hypertension will undergo MRI three times during the described diagnostic process, that is at baseline before antihypertensives are withdrawn, once antihypertensives are largely or completely withdrawn (T=1) and once patients have reached their target blood pressure (T=2). 1 year after T=2, patients will undergo a final MRI scan (T=3). In addition to MRI, during each visit patients will undergo standardised tests and questionnaires to probe cognitive and motor functioning, and lifestyle and medical information.

Study objective

Primary objectives:
1. Examine abnormalities in brain (micro)structure and vascular function in patients with hypertension aged 18-40
2. Determine the effects of blood pressure increase and subsequent blood pressure reduction during a period of withdrawal and restart of blood pressure lowering drugs on brain (micro)structure and vascular function measured with high-resolution MRI in patients with hypertension aged 18-55

Secondary objectives are:
- Investigate the effect of withdrawal and restart of antihypertensives on cognitive an motor functioning
- Explore the association between circulating markers of inflammation, including cytokines and chemokines, determined after withdrawal of antihypertensive medication, and blood pressure and brain MRI parameters
- Determine in the same patients changes in MRI parameters of brain (micro)structure and microvascular function at follow-up after 1 year
- Assess the association between cardiovascular risk factor profile and MRI parameters of brain (micro)structure and vascular function
- Determine the association between early-life hypertension and future incident clinical events

Study design

HYPERINTENSE is a prospective observational cohort study

Study burden and risks

Patients will undergo a standardized MRI protocol, vena puncture to sample blood, and standardised tests and questionnaires to probe cognitive and motor and lifestyle and medical history.
MRI is considered to be safe and without risks, as long all safety measures are adequately followed. To study the integrity of the blood-brain barrier during part of the 3 T MRI scan, patients will receive a gadolinium-based contrast agent. Side effects of injection of this contrast agent occur very incidentally and include mild effects such as nausea, headache and injection site reactions (sense of warm feeling). In case of adverse effects, patients will be treated reasonably and professionally.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Population 1: Hypertension, age between 18-40 years

Population 2: Hypertension, age between 18-55 years

(See section J. for more information)

Exclusion criteria

Pre-existing cerebrovascular disease
Pregnancy
Contraindications for 3 T MRI
Carotid artery stenosis > 50%

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	06-07-2021
Enrollment:	130
Type:	Actual

Ethics review

Approved WMO Date:	03-12-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-03-2021

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-03-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-06-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-09-2022
Application type:	Amendment
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	NL75003.091.20