Arterial spin labelling for the assessment of cerebral autoregulation - a proof of principle

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Primary Objective: • To demonstrate that changes in blood pressure and cerebral perfusion (induced with paced breathing and the Cold-pressor test) can be assessed in the MRI using the combination of NIBP and rapid ASL measurements. Secondary…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Structural brain disorders
Study type	Observational non invasive

Summary

ID

NL-OMON42505

Source
ToetsingOnline

Brief title
ASL for cerebral autoregulation

Condition

- Structural brain disorders
- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

Synonym
Alzheimer's Disease, dementia

Research involving
Human

Sponsors and support

Primary sponsor: Radboudumc
Source(s) of monetary or material Support: Alzheimer Nederland & ADDF

Intervention

Keyword: Arterial Spin Labeling, Cerebral autoregulation, Cerebral perfusion

Outcome measures

Primary outcome

• Relative cerebral blood flow changes over time (every 5s)

• Relative blood pressure changes over time (every 5s)

Secondary outcome

Feasibility:

o # of deviations from protocol

o # of motion artifacts in ASL images

o # of motion artifacts in CareTaker

Validity

o Oscillations in mean cerebral blood flow

*- rASL

*- NIRS

o Oscillations in MAP

*- CareTaker

*- Finapres

To assess the magnitude of changes that can be detected

o Variation due to physiological changes

o Variation due to measurement noise

Study description

Background summary

Cerebral hemodynamics are subject of research in many different research areas and pathologies. Cerebral autoregulation (CA), the regulatory mechanisms of the brain to maintain a constant blood flow, are an intriguing element in these cerebral hemodynamics. Cerebral autoregulation has been investigated with regard to many different pathologies, varying from traumatic brain injury to Alzheimer*s disease. Still, there are limitations regarding the assessment of cerebral autoregulation and as a result also a lack of understanding.
The tremendous increase in temporal resolution of measurements of blood flow has had a strong impact on cerebral autoregulation research [1, 2]. On the other hand, spatial resolution of these measurements has hardly increased over time. With the development of new MR sequences it is now possible to achieve a spatial resolution of several millimeters, with also a reasonable temporal resolution [3, 4]. Also MR-sequences like arterial spin labeling (ASL) are developing rapidly. Thus far, this has been at the expense of the temporal resolution to such an extent that only static CA can be assessed [5]. However, with further advancements it may already be possible to image cerebral blood flow oscillations with a temporal resolution of 0.4 Hz. We recently received a new sequence which, with further optimization is possibly able to measure oscillations in blood pressure; dynamic CA.
Also, recently, a new MR-compatible NIBP device became available, the CareTaker [6]. This suggests it may be possible to measure both oscillations in BP and in cerebral perfusion in MRI simultaneously. Together, these reflect information on the cerebral autoregulation. With the high spatial resolution of the MRI, these measurements may give additional understanding to the not so well understood mechanism of cerebral autoregulation.
However, it is not yet known what the reliability of those rapid ASL measurements is and what magnitude of changes in perfusion they are able to detect. Also, the feasibility of the MR-compatible NIBP device has yet to be proven. Since spontaneous oscillations in BP and cerebral perfusion are quite subtle, larger changes in BP and cerebral perfusion need to be induced using paced breathing and the cold pressor test (CPT) [7, 8]. These will help in assessing whether changes in cerebral blood flow will exceed the total noise of the measurements (as ASL is known to have a low signal-to-noise ratio), both for young as for elderly, who are known to have changes in their regulatory mechanisms [9].
If the measurements work in the setting proposed in this study, we will in the future be able to gain more insight in the effect of spatial differences in regulatory mechanisms. This may help in explaining why in some subjects the regulation is affected.

Study objective

Primary Objective:
• To demonstrate that changes in blood pressure and cerebral perfusion (induced

with paced breathing and the Cold-pressor test) can be assessed in the MRI using the combination of NIBP and rapid ASL measurements.

Secondary Objective(s):
• To assess whether rapid ASL measurements and NIBP measurements, using the CareTaker, are feasible to perform in a research setting
• To assess the reliability of the rapid ASL measurements and NIBP measurements, using the CareTaker
• To assess the magnitude of changes that can be detected with the rapid ASL measurements and NIBP measurements

Study design

10 healthy volunteers, aged 18 - 40 yrs and 5 healthy elderly, aged 55-75 will receive 2 measurements: one in the MRI and one within the hemodynamic lab of the department of Geriatric medicine. In both, blood pressure (CareTaker or CNAP500) and cerebral hemodynamics (either ASL or TCD/NIRS) are measured. 5-minute measurements are performed in supine position, in rest, with paced breathing (0.1 Hz) and after 2 minutes rest during 3 minutes the CPT.
Paced breathing means breathing at a pace of 6 breaths per minute (10 s for each breathing cycle), which is indicated via a screen (so subjects still breath voluntarily). This induces oscillations in blood pressure and consequently oscillations in cerebral blood flow.
The CPT is a test which activates the sympathetic nervous system by placing a subject*s hand in a bucket of ice water (0 - 5 °C). There is peripheral vasoconstriction, causing an increase in blood pressure. Also, the cerebral perfusion tends to increase. This response is consistent within a subject.

Study burden and risks

The research does not have a direct advantage for the participating subjects. However, load is minimal; total time in the MRI is approximately 30 min. There is only one visit of in total approximately 1.5 - 2 hours. All measurements are performed non-invasively and do not require big effort. The CPT is bothersome, but not related to any damage or other health risk. Therefore we would say this study is associated with *negligible risk*.

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

- Written informed consent
- Age 18-40 or age 55-75

Exclusion criteria

-Subjects who cannot have an MRI, e.g. due to claustrophobia, metal in upper body, have an implant or who suffer from epilepsy.
oIncreased risk on coronary spasms
oRecent (< 3 months) angina pectoris, myocardial infarct, brain infarct and/or heart failure.

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-12-2015
Enrollment:	15
Type:	Actual

Ethics review

Approved WMO Date:	07-10-2015
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-03-2016
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	NL54521.091.15