Empirical hemodynamic models of micro- and macro-vessels in the brain: an fMRI and RespirActTM approach

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The main objective of the study is to characterize, quantify, and model hemodynamic changes of different vessel groups in the human brain in response to external stimulation.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON45408

Source
ToetsingOnline

Brief title
Hemodynamic models

Condition

- Other condition

Synonym
Na (healthy volunteers)

Health condition

Een specifieke aandoening maakt geen onderdeel uit van dit onderzoek (gezonde vrijwilligers).

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: NIH (1R01MH111417-01)

Intervention

Keyword: fMRI, Hemodynamic modeling, Neurovascular coupling

Outcome measures

Primary outcome

Establishment and modelling (quantification) of hemodynamic changes for

different vessel groups in the human brain in response to external stimulation.

Secondary outcome

Not applicable.

Study description

Background summary

Functional Magnetic Resonance Imaging (fMRI) is the most-widely used technique to study brain function non-invasively in humans for neuroscience and in the clinic. fMRI measures brain function indirectly via local hemodynamic changes that arise from neuronal activation. Despite the wide application of fMRI, a key confound in the interpretation and quantification of the data is that the signals measured consist of a mix of hemodynamic changes, some of which relate to the vascular organization only (e.g. passive blood flow in macro-vessels), and some of which relate to the metabolic needs of active neurons (e.g. blood oxygenation changes in micro-vessels). The challenge of separating neuronally driven from purely vascular signals has inspired significant model-development work, primarily based on animal research. Translation of animal-based models to humans is however problematic due to differences in vascular anatomy and organization between species. Models tailored to the human brain will be constructed by empirical modification of animal-based models. Separation of neuronally driven and vascular signals can be achieved via reproducible inspiration of CO2 and O2 during fMRI. CO2 and O2 inspiration affects vascular signals independent of neuronal activity and is typically used to assess the reactivity of the brain vasculature. Delivery of CO2 and O2 will be controlled digitally by continuous analysis of expiratory gas and model controlled

inspiration of O2 and CO2 to achieve a reliable and repeatable gas delivery using the RespirActTM. The measurements will be performed at 3 Tesla (T) and 7T. The vascular source of the fMRI signal is different at 7T as compared to 3T due to the magnetic properties of blood and increased signal-to-noise. Detailed 7T measurements will link to the detailed analysis and models available from animal research, and will in turn be used to translate models to the widely available 3T scanners. The models will be tested in a separate group of subjects for a range of neuronally driven signals without respiratory challenge.

Study objective

The main objective of the study is to characterize, quantify, and model hemodynamic changes of different vessel groups in the human brain in response to external stimulation.

Study design

Subjects will be included in a descriptive study for hemodynamic models of the MR signal. The study involves two parts involving two subject cohorts. Part I: fMRI with one simple task and respiratory challenge (n=28), part II: fMRI with several simple tasks without a respiratory challenge (n=28). In part I, parameters describing hemodynamics due to vascular (respiratory challenge) and neuronal (simple task) processes will be extracted and modelled. In part II, the parameters modelled will be tested for several simple tasks.

Study burden and risks

No benefits are expected for the volunteers. There are no known risks associated with fMRI acquisition and the burden can be considered minimal. Two or three visits will be required per subject.
Respiratory challenge: The controlled gas breathing requires a closed breathing system and subjects have to breathe through a mask. Further, subjects may experience discomfort due to the increased levels of CO2 in the blood. However, end-tidal CO2 partial pressure levels of 40-57 mmHg (+5 - 10 mmHg above the subjects* baseline value) are in physiological ranges and are experienced repeatedly by most people over the day and during exercise. If subjects experience discomfort because of high CO2 levels, they can open a valve in the mask or we can switch immediately to 100% oxygen by pushing the red button on the front of the gas blender. In the MRI, they can squeeze the emergency button. Subjects can terminate the study at any time by communicating with the operator. Approximately 6.5% (11 out of 168) of the subjects may experience breathing discomfort during CO2 inhalation and terminate the study, and approximately 8.9% (15 out of 168) of the subjects may experience breathing discomfort and claustrophobia during CO2 inhalation and terminate the study, as reported in previous studies conducted at the University Medical Center (UMC)

Utrecht. Risks associated with controlled gas breathing of high levels of CO2 with the RespirActTM are minimal because the minimum O2 level in all the gas mixtures is 10%. The blood gas is controlled by a digitally controlled gas blender steered by end-tidal blood gas pressure CO2 and O2. So, CO2 and O2 levels and breathing frequency are monitored online. An independent blood oxygen saturation and respiratory rate monitoring will be performed during the MRI measurements with fingertip pulse oximetry and a pressure sensor for the respiratory rate. All staff that will operate the RespirActTM will be trained by an experienced operator certified by the manufacturer.

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

- Informed consent;

- 18 years or older.

Exclusion criteria

Part I (fMRI with RespirAct):
- Standard contra-indications for 3T or 7T MRI scanning;
- Unwilling or unable to co-operate with breathing manoeuvres;
- Respiratory or cardiac limitations to breathing at 20 L/min;
- Medical contra-indications to limited hypercapnia or hypocapnia (known increased intracerebral pressure, metabolic acidosis or alkalosis);
- Known vascular brain disease.;Part II (fMRI without RespirAct):
- Standard contra-indications for 3T or 7T MRI scanning.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-03-2018
Enrollment:	56
Type:	Actual

Medical products/devices used

Generic name:	RespirActTM
Registration:	No

Ethics review

Approved WMO Date:	19-04-2017
Application type:	First submission
Review commission:	METC NedMec

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	NL60115.041.16