Protein-specific turnover in the human brain; Measuring protein-specific synthesis rates of the human brain using the D2O dosing method

Published: 18-10-2017
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To assess protein-specific synthesis rates neocortex, hippocampus, temporalis muscle, and vastus lateralis muscle using the D2O dosing method.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Musculoskeletal and connective tissue disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON55574

Source
ToetsingOnline

Brief title
D2O in Brain

Condition

- Musculoskeletal and connective tissue disorders NEC
- Neurological disorders NEC

Synonym
Brain diseases, Temporal Lobe Surgery

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Brain protein synthesis, Protein synthesis, Protein turnover

Outcome measures

Primary outcome

Primary study parameters include protein synthesis rates and enrichments of

neocortex, hippocampus, temporalis muscle, and vastus lateralis muscle.

Secondary outcome

Secondary parameters include whole-body protein synthesis, breakdown,

oxidation, and net balance.

Study description

Background summary

Brain plasticity is defined by a dynamic balance between protein synthesis and protein breakdown rates. Recently, human brain tissue from a pilot project has shown to turn over at a rate of ~3% per day using contemporary stable isotope methodology. However, assessment of these turnover rates represents the integrated synthesis rates of all available protein in brain tissue and does not allow assessment of synthesis rates on the level of individual proteins. Therefore, this project will apply the D2O dosing method primarily to assess protein turnover rates of different parts of the human brain. In addition, using D2O methodology will enable us to assess protein turnover on the level of individual proteins.

Study objective

To assess protein-specific synthesis rates neocortex, hippocampus, temporalis muscle, and vastus lateralis muscle using the D2O dosing method.

Study design

Explorative study design.

Study burden and risks

The risks involved in participating in this study are minimal. We will only make use of tissue that is being resected as part of the surgical procedure. Saliva sampling is risk-free and blood sampling is minimal (8-12 x 10mL total) and will be conducted using catheter placement during the dosing day and the day of the surgical procedure (1 blood sample and 4-8 samples, respectively). The vastus lateralis biopsy will be obtained by an experienced physician during the surgical procedure using the Bergström percutaneous needle biopsy method.

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
* Male and female patients scheduled for temporal lobectomy
* Age 18 - 65 years
* Compos mentis

Exclusion criteria

* Comorbidities and neuromuscular disorders of the lower limbs severely interacting with mobility, with limited or no opportunity for improvement (e.g. cerebral palsy)
* Peripheral artery disease Fontaine III or IV
* Chronic Obstructive Pulmonary Disease (COPD) GOLD III or IV
* Use of systemic steroids in the past four weeks, other than indicated for the specific type of surgery
* Use of anti-inflammatory biologicals (e.g. TNF-alfa blockers) in the past four weeks
* Surgical intervention in the past four weeks
* Total parenteral nutrition at day of surgery
* Pregnancy
* Neoadjuvant chemotherapy or radiotherapy

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-10-2018
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO Date:	18-10-2017
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	17-11-2020
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL63300.068.17