The impact of gender differences in P-glycoprotein function measured with [18F]MC225 and PET

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The main objective of this study is to investigate gender differences in P-gp function at the blood brain barrier, in order to gain further insight into the impact of these differences on the action of pharmaceuticals (antidepressants and...

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

Summary

ID

NL-OMON53850

Source
ToetsingOnline

Brief title
Genderdifferences in P-gp function

Condition

- Other condition

Synonym
genderdifferences

Health condition

transporterfunctie op de bloed-hersenbarriere

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Gratama Subsidie;PUSH Siemens Healthineers,Siemens Healthineers

Intervention

Keyword: - Blood-brain barrier, - Gender differences, - Neuropsychiatric disease, - P-glycoprotein

Outcome measures

Primary outcome

PET images will be analysed using PMOD software (PMOD technologies, Zurich, Switzerland, version 4.1). Predefined brain regions based on a maximum probability map are selected as volumes of interest (VOIs). Tracer kinetics of [18F]MC225 reflect the BBB P-gp function and will be assessed as outcome measure for P-gp efflux function. Those will be compared in between the groups of male and female subjects.

Secondary outcome

not applicable

Study description

Background summary

P-gp is one of the main efflux transporters at the blood-brain barrier and is responsible for the transport of a variety of neurotoxic substances, including pharmaceuticals. Multiple studies report gender differences in therapeutic outcomes, toxicity and side effects for many drug agents. P-gp plays an important role in the bio-availability, drug distribution, metabolism and elimination of pharmaceuticals labelled as P-gp substrates (e.g. the majority of antidepressants and antipsychotics). A difference in P-gp function was already reported in hepatic P-gp expression. The aim of the current study is to evaluate the influence of gender on cerebral P-gp function. Outcomes of this

study can be of great importance in gender-based prescription of P-gp substrate pharmaceuticals.

Study objective

The main objective of this study is to investigate gender differences in P-gp function at the blood brain barrier, in order to gain further insight into the impact of these differences on the action of pharmaceuticals (antidepressants and antipsychotics) in the brain.

Study design

10 healthy volunteers (5 male, 5 female subjects) will undergo a 60 minute dynamic [18F]MC225 PET scan with arterial sampling. Design: observational study.

Study burden and risks

[18F]MC225, a weak P-gp substrate, proved a suitable tracer for PET imaging and quantification of the P-gp transporter in animal (rat and NHP) studies. Since [18F]MC225 is a PET tracer, the mass of the injected drug is very low (<=100 µg) and no pharmacological effect of [18F]MC225 is expected. In recent human studies in healthy volunteers no side effects were reported. Study subjects will receive a low dose of radiation during the PET scans. The total effective dose is established by a radiation expert and is 3.3 mSv, which is below the effective annual radiation dose limit of 20 mSv/y.

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

- Age: 50-80 years
- MMSE: 28-30
- No history of any neuropsychiatric disorders that might affect the P-gp function or blood-brain barrier integrity

Exclusion criteria

- Use of medication with known P-gp affinity
- History of neuropsychiatric disorders affecting the P-gp function or blood-brain barrier integrity

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2023
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	[18F]MC225
Generic name:	[18F]MC225

Ethics review

Approved WMO Date:	12-04-2023
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-11-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-12-2023
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2022-003664-25-NL
CCMO	NL83060.042.22