# PET imaging of the noradrenaline system in different neurodegenerative conditions

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Other condition |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON51069

**Source**
ToetsingOnline

**Brief title**
JPND HEROES

### Condition

- Other condition
- Chromosomal abnormalities, gene alterations and gene variants
- Movement disorders (incl parkinsonism)

**Synonym**
dementia, parkinson's disease

**Health condition**

neurodegeneratieve aandoeningen (ziekte van Alzheimer)

**Research involving**

Human

## Sponsors and support

**Primary sponsor:** Universitair Medisch Centrum Groningen
**Source(s) of monetary or material Support:** ZonMW

## Intervention

**Keyword:** 11C-methylreboxitine, locus coeruleus, noradrenaline, positron emission tomography

## Outcome measures

### Primary outcome

Several values will be computed from the PET data and between group results are statistically compared: NET binding potentials (BP) will be computed for each region of interest (LC and projection areas), .and between-group differences will be investigated.

### Secondary outcome

Correlations between results on the MMSE, NPI, PSQI, ADL en iADL scales and the noradrenaline activity will be investigated. We will also look for between-group differences.

# Study description

### Background summary

Noradrenaline (NA) is produced in the brain in the locus coeruleus (LC). NA and its reuptake system, the noradrenaline transporter (NET), are implicated in a wide range of cognitive functions, including attention, memory, and arousal. As a result, the NA system is also of great interest in the context of neurodegenerative disease such as Parkinson*s disease, Alzheimer*s disease, and Alzheimer's dementia in Down syndrome, where such cognitive functions are compromised. Recently, the identification of a suitable radiotracer for imaging the NET using positron emission tomography (PET) has received growing

attention. The use of such a PET radiotracer enables the study of the NET system in vivo. The most suitable of the currently available radiotracers is [11C]methylreboxetine ([11C]MRB). [11C]MRB is being used worldwide in a growing number of clinical studies.

### Study objective

The aim of this study is to determine NET availability in patients with neurodegenerative diseases to characterize NA system degeneration in people with Alzheimer's disease, Parkinson's disease (with and without dementia) and with Downsyndrome (with and without dementia). We hope that the results of this study can help us develop a novel diagnostic tool and a starting point for developing new therapeutic treatments.

### Study design

This study will use PET imaging with the [11C]MRB radiotracer allowing in vivo examination of NET availability in the locus coeruleus and key projection areas (cortex, hippocampus). To be able to interpretate the PET data, MRI images of the brain are needed. Furthermore we will perform a few assessments to determine cogntive functioning and sleep behaviour (MMSE, NPI, PSQI, ADL and iADL scales).

### Study burden and risks

This study entails a minimum risk to the participants. In general, PET imaging is a procedure with minimal adverse effects. Intravenous injection of the tracer is minimally invasive. The concentration of the [11C]MRB tracer used in this study does not have a pharmacological effect nor is it expected to cause adverse effects. Participants do not directly benefit from the study. Outcomes of this study will contribute to development of new diagnostic methods and possibly therapeutic methods in the furture.

## 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

all participants:
•age between 50 - 80 years

Healthy volunteers:
•Willingness to cooperate and sign written informed consent.

Participants with Alzheimer's disease:
•Diagnosis of AD according to the criteria from the National Institute on Aging-Alzheimer*s Association (NIA-AA)
Willingness to cooperate and sign written informed consent.
•MMSE score between 18-26 (inclusive);

Participants with Parkinson's disease
• Willingness to cooperate and sign written informed consent.
•Diagnosis of PD according to the London Parkinson*s disease society brain criteria

Participants with Parkinson's disease and dementia:
• Willingness to cooperate and sign written informed consent.
•Diagnosis of PD according to the London Parkinson*s disease society brain criteria
• MMSE score between 18-26 (inclusive);

Participants with Down Syndrome:

•availability of a caregiver/proxy who will be present at visits.

Participants with Downsyndrome & dementia
•availability of a caregiver/proxy who will be present at visits.
•A Clinical diagnosis of AD based on the Dementia Scale for Down Syndrome (Gedye A., 1995. Dementia Scale for Down Syndrome. Vancouver, BC: Gedye Research and Consulting) and on the Behavioral and Pyschological Symptoms of Dementia in Down Syndrome (BPSD-DS) scale (Dekker A.D. et al., 2018) developed by our group and recently optimized (in press, Dekker A.D. et al., 2021).

## Exclusion criteria

All participants:
•usage of any medication that affects the noradrenaline system
•Pregnancy
•Contra-indications for MRI or PET (such as claustrophobia)
• brain MRI evidence of any structural abnormality, such as major stroke or mass that is likely to interfere with the interpretation of the PET scan;
•Past or present developmental disorder or psychiatric disorder (expect for Down's syndrom)

Healthy volunteers:
• Abnormal results on the Mini-Mental State Examination (MMSE) (<27);
• (Subjective) memory complaints;
• Absence of signed informed consent form

Participants with Alzheimer's Disease:
• History of neurological conditions other than AD;
• Absence of signed informed consent form

Participants with Parkinson's disease
• History of neurological conditions other than PD;
• Absence of signed informed consent form
• Past or present developmental disorder or psychiatric disorder

Participants with Parkinson's disease and dementia:
• History of neurological conditions other than PD-D;
• Absence of signed informed consent form.

Participants with Down's Syndrome:
• Absence of signed informed consent form or of caretaker/study partner (proxy

consent and assent).

Participants with Down's syndrome & dementia
• Absence of signed informed consent form or of caretaker/study partner (proxy consent and assent).

# Study design

## Design

**Study type:** Observational invasive

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

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 01-04-2018 |
| Enrollment: | 50 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | [11C]-methylreboxitine |
| Generic name: | [11C]-methylreboxitine |

# Ethics review

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|---|---|
| Approved WMO Date: | 04-01-2022 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |
| Approved WMO Date: | 22-02-2022 |

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|---|---|
| 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 | EUCTR2021-002489-42-NL |
| CCMO | NL77767.042.21 |