

# NephroX 2, Neural control of kidney oxygenation

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To establish the role of renal sympathetic modulation on renal blood flow, metabolism and oxygenation we propose three closely related series of experiments. Group 1: Sympathoactivation in healthy humans 12 healthy volunteers will undergo a graded...

<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruitment stopped
<b>Health condition type</b>	Nephropathies
<b>Study type</b>	Observational invasive

## Summary

### ID

NL-OMON42410

### Source

ToetsingOnline

### Brief title

NephroX 2

### Condition

- Nephropathies
- Vascular hypertensive disorders

### Synonym

nephrosclerosis; high blood pressure

### Research involving

Human

### Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum

**Source(s) of monetary or material Support:** ZonMW Klinisch Fellowship

## Intervention

**Keyword:** Kidney, MRI, oxygenation

## Outcome measures

### Primary outcome

Intra individual changes in renal desoxygenation, metabolism and renal blood flow.

### Secondary outcome

Change in intra individual changes in renal desoxygenation, metabolism and renal blood flow.

## Study description

### Background summary

Although many primary kidney diseases can be adequately managed on themselves (i.e. diabetes, hypertension, glomerulonephritis), minor injury may often still lead to renal failure in the long run. To this end, there is a pressing need to obtain a more detailed understanding of cause(s) and mechanisms underlying the progression from minor loss of function to complete renal failure. Multiple forms of acute and chronic kidney disease are associated with a relatively low tissue oxygen tension (pO<sub>2</sub>) within kidney, i.e. hypoxia. This has led to the proposition that renal parenchymal hypoxia is not just a consequence of kidney disease, but rather a common pathogenic event in several forms of kidney disease.

There is substantial evidence from animal models of hypertension and/or CKD that the kidney branches of the sympathetic nervous system are a modulator of renal blood flow and tubular sodium reabsorption and thus determine the intrarenal balance between oxygen supply and demand. In humans however, the effects of sympathetic modulation on kidney oxygenation have not yet been established.

Recently we developed an MRI sequence that includes assessment of renal oxygenation with Blood Oxygen Level-Dependent (BOLD) MRI, renal blood flow and metabolism. This enables quantification of changes in kidney flow and oxygenation during acute and chronic modulations of renal sympathetic

activity:

## **Study objective**

To establish the role of renal sympathetic modulation on renal blood flow, metabolism and oxygenation we propose three closely related series of experiments.

Group 1: Sympathoactivation in healthy humans 12 healthy volunteers will undergo a graded lower body negative pressure (LBNP) challenge (0, 10, 20, 30 mmHg for 15 minutes per step) during MRI scanning. This is a standardised method to induce a graded induction of sympathetic activity. During each step kidney oxygenation and flow will be assessed using MRI.

Groups 2a/2b: Chronic renal sympatho-inhibition by surgical denervation We will measure renal blood flow and oxygenation using MRI during a graded lower body negative pressure challenge in 12 living donor/recipient kidney transplantation couples. Donor will undergo this testing before and after the donation procedure and the recipients on two specified timepoints after transplantation.

## **Study design**

Prospective etiological study

## **Study burden and risks**

Individual subjects will gain no direct benefit from this study, there is however direct group related benefit for kidney donors and transplant recipients (groups 2a/b; identifying potential pathways underlying increased risk for chronic kidney disease after transplantation, respectively allograft nephropathy)

There are no risks involved in the MRI scanning (All groups)

The risk of the LBNP challenge is occurrence of a vasovagal reaction (<10%; \*matige kans\*), which is a benign event (\*matige schade\*). This risk (\*matig risico\*) is minimized by using a relatively limited LBNP challenge, monitoring of blood pressure and heart rate and direct observation of the subject during the LBNP challenge.

## **Contacts**

### **Public**

Academisch Medisch Centrum

Meibergdreef 9  
Amsterdam 1105AZ  
NL  
**Scientific**  
Academisch Medisch Centrum

Meibergdreef 9  
Amsterdam 1105AZ  
NL

## Trial sites

### Listed location countries

Netherlands

## Eligibility criteria

### Age

Adults (18-64 years)

Elderly (65 years and older)

### Inclusion criteria

#### 5.1 Population

Group 1: 12 healthy volunteers aged \* 18 years

Group 2a: 12 living kidney donors

Group 2b: 12 kidney transplant recipients;

5.2 Inclusion criteria  
In order to be eligible to participate in this study, a subject must meet all of the following criteria:

- General inclusion criteria

\* age \*18 years

\* able to give informed consent

### Exclusion criteria

5.3 Exclusion criteria;  
o General exclusion criteria (for volunteers and patients):

\* not willing to be informed about unexpected findings during the study

\* (possible) pregnancy or lactation

\* known or suspected diseases or conditions that could interfere with the study

\* Contra-indications to MRI (for volunteers and patients), based on current practices,

including:

- \* Claustrophobia

- \* metal implants, devices etc.: endoprosthesis, pacemaker, birth control device (IUD), neurostimulator, insulin pump, intra-ocular metal particles, metal heart valve, cochlear implant;

o Group specific exclusion criteria:

Group 1

- \* use of any prescribed medication (excl. contraceptives) and home use of NSAID\*s during the study

- \* body mass index >30

- \* diagnosed hypertension or hypertension (>140/90mmHg) upon screening

- \* smoking;

Group 2a

- \* matching kidney transplant recipient not willing to participate;

Group 2b

- \* matching kidney transplant donor not willing to participate

- \* absolute contraindications for short-term blood pressure perturbations

## 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): 15-04-2016

Enrollment: 36

Type: Actual

## Ethics review

Approved WMO

Date: 24-07-2015

Application type: First submission

Review commission: METC Amsterdam UMC

## 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	NL53367.018.15

## Study results

Date completed:	03-11-2017
Actual enrolment:	8