Gut Microbiome Analysis in de Novo Parkinson's Patients

Published: 21-08-2017
Last updated: 12-10-2024

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Movement disorders (incl parkinsonism)
Study type	Observational invasive

Summary

ID

NL-OMON50393

Source
ToetsingOnline

Brief title
DUPARM

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's Disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,Reeds verworven fondsen als vergoeding voor eerder uitgevoerd contractresearch

Intervention

Keyword: Dopaminergic medication, Gut Microbiota, Parkinson's Disease, Treatment naïve

Outcome measures

Primary outcome

Taxonomic classification of fecal microbiota composition through high-throughput sequencing and analysis of the 16S ribosomal RNA gene or metagenomic shotgun sequencing. At a later stage the gut microbiota of left over material can be assessed using other -omics methods.

Secondary outcome

Secondary outcome parameters include the presence and extend of (prodromal) PD symptomatology, specific treatment protocols and possible confounders influencing microbiota composition, including clinical-genetic PD subtypes, colon transit time, systemic inflammation and intestinal wall permeability.

Study description

Background summary

Recent studies indicate a significant difference in gut microbiota composition between PD patients and healthy controls. However, since the vast majority of included patients in these studies were using dopaminergic medication, no inferences could be made concerning the possible downstream effects of dopaminergic medication on gut microbiota composition. Here, we will determine the relative contributions of PD diagnosis and dopaminergic medication on microbiome composition through investigation of gut microbiota composition of initially treatment naive PD patients at baseline and after one- and three-years follow-up.

Study objective

The primary objective of this study is to determine the relative contributions of PD diagnosis and dopaminergic medication use to the changes in microbiota

composition observed in PD patients. Secondary objectives are to determine the relative contributions of other possible confounders, to microbiota composition variability in PD patients.

Study design

We propose a case control study with a prospective outlook to compare changes in microbiota composition between de novo PD patients without a history of dopaminergic medication use and healthy age, sex and constipation matched controls. Microbiota composition of said cohort of PD patients will again be assessed after one year of dopaminergic medication use to establish the effect of dopaminergic medication on microbiota composition. Both groups will be assessed on in- and exclusion criteria, including motor and non-motor symptomatology associated with (prodromal) PD and factors influencing gut microbiota composition, using questionnaires.

Study burden and risks

The burden associated with participation consists of collecting a stool sample using a stool sample collection kit and filling out the provided questionnaires, which will take a total of about 1 hour. From participants willing to participate in the genetic screening of genome-wide variants and/or whole gene sequencing of the GBA1 gene, a saliva sample will be collected. Participants willing to participate in the intestinal wall permeability assessment will collect urine over a 24-hour period after ingestion of a standardized sugar solution. The first five hours of urine collection, the participant will fast, except for water consumption. Also, 30ml of blood will be collected for markers of intestinal wall permeability and associated intestinal inflammation. Additionally, one visit to the UMCG will take place to assess the UPDRS and MoCA and collect blood (from participants of the intestinal wall permeability assessment). This will be done during the same visit as in which an F-DOPA PET scan will be performed, if warranted, as part of the diagnostic workup (total dosage 6.7mSv). If no other visits to the UMCG are planned and the participant does not take part in the intestinal wall permeability assessment, all assessments can also be done from home. The additional time needed for the purpose of this study will be a maximum of 2 to 3 hours at baseline spread out over multiple days. After one year, PD subjects will be asked to hand in another fecal sample and fill out the stool diary and food questionnaires. This will take approximately 40 minutes, whereas the clinical assessments take about 20 minutes. After three years, the entire baseline will be repeated. In addition, PD participants can opt-in for (1) optional withdrawal of 60mL of blood for the assessment of intestinal wall permeability similar to the baseline, as well as systemic inflammation, single-cell RNA sequencing (sc-RNAseq) of peripheral blood mono-nuclear cells (PBMCs) and glucocerebrocidase (GCase) activity; and (2) optional measurement of colonic transit time using radio-opaque markers and an abdominal CT

(3.5mSv). The total workload of the study is therefore 5-7 hours spread out over multiple days and visits. The associated risk is negligible and there are no benefits associated with participation.
To make any inferences concerning a possible role of the microbiome in the pathophysiology of PD or as an early marker of disease, it is essential to establish the relation between PD diagnosis and gut microbiome composition without the possible confounding effect of dopaminergic medication. For this purpose, it is a necessity to compare the gut microbiota composition of treatment naïve PD patients to healthy age-,sex- and constipation-matched controls. Furthermore, determination of the gut microbiome composition after one and three years will aid in quantifying the extent to which dopaminergic medication use might alter gut microbiota composition and allows for PD subtype comparisons in relation to disease progression.

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:
- Written informed consent
Study group:
- Diagnosed Parkinson*s disease according to the UK Parkinson*s Disease Society Brain Bank Criteria
Control group:
- Healthy sex- and age-matched controls, also matched according to presence and severity of constipation.

Exclusion criteria

All participants:
Gastrointestinal exclusion criteria:
- Active or persistent primary disease of the gastrointestinal tract
- History of peritonitis, severe endometriosis, abdominal, intestinal or urogenital fistula,
- Hepatobiliar or pancreatic disease (except asymptomatic cholecystolithiasis)
- History of abdominal or anorectal surgery, except minor surgery such as uncomplicated appendectomy or cholecystectomy (>6 months ago)
- Severe gynaecological prolapse (grade III)
- Cancer and/or adjuvant treatment within the last 6 months
- Within the last three months: narcosis, analgosedation, endoscopic procedure of the gastrointestinal tract, abdominal trauma
- Within the last three months: gastrointestinal tract infection, food intoxication,
Study group:
- History of dopaminergic medication use
Control group:
- History of neurodegenerative disease, in particular signs of parkinsonism.
- Probable prodromal PD. Controls will, however, be matched according to presence and severity of constipation as a possible confounder.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-10-2017
Enrollment:	480
Type:	Actual

Ethics review

Approved WMO Date:	21-08-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-12-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-01-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-10-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-01-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	10-06-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-10-2024
Application type:	Amendment
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
CCMO	NL61123.042.17