Linking protein profiles to disease progression and clinical expression in Parkinson*s disease

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We aim to identify CSF and serum proteins in PD patients that are associated with disease progression and/or clinical phenotypic variations and serve to distinguish between PD and other Parkinsonian syndromes.

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

Summary

ID

NL-OMON33857

Source
ToetsingOnline

Brief title
Protein expression in Parkinson's disease

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's disease; movement disorders

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Parkinson Vereniging

Intervention

Keyword: Biomarker, CSF, Parkinson's disease, Protein expression

Outcome measures

Primary outcome

A lumbar puncture and a venous blood puncture will be performed in all patients and controls. For the subsequent analysis of CSF and serum samples, we will use a parallel approach. Previously discovered PD-related proteins will be validated in CSF and blood samples of PD patients, patients with parkinsonian symptoms not related to Parkinson*s disease and healthy controls using enzyme-linked immunosorbent assays (ELISAs) and Western Blotting. For the PD patients, we will analyze the association between CSF and serum proteins and clinical characteristics. In addition, we will perform state-of-the-art proteomics in order to discover new candidate biomarkers: proteins in CSF of eight early-stage PD patients, eight moderately advanced cases, eight advanced cases, and eight controls will be identified and quantified with stable isotope labelling (iTRAQ) in conjunction with multidimensional liquid chromatography coupled to tandem mass spectrometry. The newly discovered proteins will subsequently be validated in both CSF and blood samples of PD patients with various disease stages and clinical expression, patients with parkinsonian syndromes and control patients to evaluate the specificity of sensitivity of these potential biomarkers for PD, PD progression and PD phenotypes.

Secondary outcome

not applicable.

Study description

Background summary

Diagnosing Parkinson*s disease (PD), a disease affecting more than 4 million people worldwide, can be very difficult in its early stages. Many other parkinsonian syndromes, including vascular parkinsonism, progressive supranuclear palsy (PSP) and multiple system atrophy (MSA), can mimic PD. Cerebrospinal fluid (CSF) and serum proteins may serve as clinical biomarkers and increase the accuracy of an early clinical diagnosis of PD. In addition, they may enable us to monitor disease progression and give new insights into molecular processes involved. The clinical expression and rate of progression of is highly variable from one patient to another. Much is unknown about the relation between the rate of progression and the clinical expression of PD. Moreover, it is, yet unknown whether the clinical expression of PD is the result of various sequential pathological processes in the peripheral and central nervous system. Specific and sensitive biomarkers may give new insight in the various clinical phenotypes and disease progression.

Study objective

We aim to identify CSF and serum proteins in PD patients that are associated with disease progression and/or clinical phenotypic variations and serve to distinguish between PD and other Parkinsonian syndromes.

Study design

cross-sectional.

Study burden and risks

For patients, procedures for the study will be combined with a regular visit to the outpatient clinic for movement disorders. The procedures for this study for newly presenting patients, i.e. venous blood puncture and lumbar puncture, will take approximately 30 minutes. Patients already under treatment at the outpatient clinic will be clinically characterized by means of questionnaires, cognitive testing and clinical examination. These procedures will take 1,5 hours at the outpatient clinic and 2 hours at home to fill in the questionnaires.
For controls, procedures consist of a general neurological examination, cognitive testing, venous blood puncture and lumbar puncture with a total duration of approximately 90 minutes.
Risks associated with venous blood puncture include haematomas and incidentally infections. Risks associated with lumbar puncture include post lumbar puncture headache, infection and haemorrhage. These risks will be minimized by the

applied puncture procedures.

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

PATIENTS
(1) Patients of the outpatient clinic for movement disorders with a suspected parkinsonian syndrome, based upon the presence of at least one of the following parkinsonian symptoms: hypokinesia, bradykinesia, rigidity, tremor or postural instability.
(2) Patients already under treatment at the outpatient clinic for movement disorders and diagnosed with PD or one of the following other parkinsonian syndromes: MSA, PSP, vascular parkinsonism.
(3) Being able to understand the aim of the study and the study procedure and give written informed consent;HEALTHY CONTROLS

Being able to understand the aim of the study and the study procedure and give written informed consent

Exclusion criteria

PATIENTS
(1) A history of neurological disorders other than a parkinsonian syndrome, that affect the central nervous system or are known to influence CSF proteins
(2) Use of anticoagulants or indications for coagulation disorders
(3) Infected skin over the needle entry side for lumbar puncture
(4) Signs of raised intracranial pressure
(5) Unwillingness to be informed of unexpected medical findings;HEALTHY CONTROLS
(1) A history of neurological disorders that affect the central nervous system or are known to influence CSF proteins
(2) Abnormal findings at general neurological examination
(3) Use of anticoagulants or indications for coagulation disorders
(4) Infected skin over the needle entry side for lumbar puncture
(5) Signs of raised intracranial pressure
(6) Unwillingness to be informed of unexpected medical findings

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-09-2008
Enrollment:	282
Type:	Actual

Ethics review

Approved WMO Date:	10-07-2008
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	NL23401.029.08