The attenuation coefficient of the retinal nerve fiber layer derived from spectral domain optical coherence tomography AND diplopia in Parkinson*s disease

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

Summary

ID

NL-OMON44886

Source
ToetsingOnline

Brief title
New OCT technique and diplopia in Parkinson's disease

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's disease; Idiopathic parkinsonism

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W,Wij zijn in gesprek met het internationaal Parkinson fonds

Intervention

Keyword: diplopia, optical coherence tomography, Parkinson's disease, retinal nerve fiber layer

Outcome measures

Primary outcome

Part 1: The main study parameter is the RNFL-ac and its association with the

presence of PD will be investigated.

Part 2: The main study parameter is diplopia and its association with the

presence of PD will be investigated.

Secondary outcome

Secondary parameters are the RNFL thickness and local differences of the

RNFL-ac of the retina and diplopia. The association with these parameters and

the presence of PD will be investigated.

Other study parameters are age, sex, ethnicity, and MMSE score, and for PD

patients also UPDRS score and modified Hoehn and Yahr stage (C1 protocol,

Appendix C), years from diagnosis and the use of dopaminergic medication.

There are no secondary endpoints.

Study description

Background summary

An clinical diagnosis of Parkinson*s disease (PD) is still challenging, in particular in the early stages. A quarter of patients is initially misdiagnosed, even when seen by movement disorder specialists.1 An accurate diagnosis is a prerequisite for adequate patient counseling and the start of

therapy. PD is now known to be a multisystem disorder that includes retinal pathology and visual complaints like diplopia.2,3 With the development of Optical Coherence Tomography (OCT) in vivo visualization of the retina is possible and recent studies using this technique have shown that the Retinal Nerve Fiber Layer (RNFL) in PD is significantly thinner than in healthy subjects.4,5 However, since the observed differences are small with overlapping confidence intervals, it is unlikely that regular RNFL measurements will prove useful as an (early) diagnostic tool.
A possible solution comes from research in glaucoma patients, in whom atrophy of the RNFL reflects disease progression.6 In glaucoma patients, measurement of the RNFL attenuation coefficient (RNFL-ac), which reflects the scattering properties of the retina, proved to be a sensitive measure of RNFL changes in addition to the usual RNFL-thickness,7 see figure 1. Whether this novel method of measuring RNFL properties is also useful in patients with PD has never been investigated.
In this pilot study we want to study the differences in RNFL-ac between PD patients and healthy controls. When RNFL-ac proves to be a sensitive measure of retinal pathology in PD it would have great potential as a powerful and non-invasive diagnostic tool to differentiate between PD patients and healthy subjects. If it proves to be highly sensitive it might be able to differentiate between PD patients and healthy subjects in a very early stage, maybe even before motor symptoms of PD are present. Furthermore it might be a biomarker for disease progress in PD patients, which can be valuable in monitoring the effect of future protective therapy.
In addition we will investigate visual complaints in PD patients and investigate the difference with healthy controls. PD patients have impaired mobility and visual compensation is important to prevent falling.3 Many PD patients complain about dubbel vision which is poorly understood. To the authors knowledge there is never been a study with orthoptistic investigation of PD patients. We want to perform a orthoptistic investigation in PD patients to objectivate the dubbelvision and compare these findings to those in healthy controls

Study objective

Part 1: The primary objective is to investigate if the RNFL-ac in PD patients differs significantly from the RNFL-ac in healthy controls.
Secondary Objectives are:
1) to investigate if the RNFL-ac can be used to differentiate PD patients from healthy controls.
2) to compare the sensitivity of the RNFL-ac with RNFL thickness in differentiating PD patients from healthy controls.
3) to investigate local differences in the RNFL-ac of the retina.

Part 2: The primary objective of the second part of the study is to objectivate dubbelvision in PD patients and compaire its occurrence to healthy controls
Secondary objectives of the second part of the study are

1) Investigate visual acuity in PD patients and compare this tho the visual acuity in healthy controls
2) Investigate astigmatism in PD patients compared to astigmatism in healthy controls

Study design

This pilot study is an observational, cross-sectional study in PD-patients and healthy control subjects. The study duration is 1 year and the study will take place in the OLVG in Amsterdam.
The study protocol starts with a clinical examination and a visual acuity test (with a Snellen chart) by a neurologist with experience in movement disorders (AMMV, JLMvHH or HCW) to confirm the clinical diagnosis of PD. This will take up to 20 minutes.
After an optional 10-minutes break patients and controls will undergo the Ophtalmologic examination. This consists of an ocular pressure examination, slit lamp examination, fundoscopy and OCT, and will take another 70 minutes. In total (including the break) the protocol takes 1 hour and 40 minutes.

Study burden and risks

An information letter of this study (see METC protocol, Appendix D) will be given or sent to PD patients attending the out-patient clinic of the OLVG. After informed consent eligible patients will be invited to participate in the study protocol.

The study protocol begins with a clinical examination: a regular neurological examination including a MMSE, and a visual acuity test (with a Snellen chart), performed by a movement disorder specialist (AMMV, JLMvHH or HCW). The clinical examination will take place in the ophthalmology outpatient clinic of the OLVG and will take 20 minutes.
After an optional 10-minute brake the ophthalmologic examination will start. Both eyes of the subject will be examinated. First ocular pressure will be measured by non-contact tonometry. For this the subjects will be seated in a chair and rest their chin on a holder. They will be asked to look at a green light and will feel a puff of air in their eyes, one by one. This is not painfull and there will be no direct contac with the eyes of the subjects.
After this an OCT scan of the retina will be done, with the Spectralis OCT system (Heidelberg Engineering, Dossenheim, Germany). For this subjects will also be seated in a chair and rest there chin on a holder. They will be asked to look at a red infrared light, again there will be no direct contact with the subject eyes and there is no potential harm of this test. The reflection of the infrared light in the subject eyes will be processed by the OCT machine. In the second part of the study an orthoptist will investigate the subject which wil take 20 minutes. The subject will be seated in a chair again and will be asked to look at a screen on eye level.The subject will be asked to wear glasses with

one green and one red glass and to hold a green flashlight. Then there will be a red light projected on the screen and the subject is asked to point the green fleshlight exactly on the red light on de screen. The accuracy with which the subject is able to do this will be measured.
The next step in the study protocol is to giveAfter this the subject will get eye dorrps to achieve mydriasis. Every subject will get one drop of tropicamide 1%, and in case of dark eyes, an additional drop of fenylefrine 5%. These eye drops may give transient side effects: tropicamide may give a prickling feeling, a raised ocular pressure, blurring of vision, dry mouth, headache, tachycardia, allergic reaction and although rare and mainly in children, a psychotic episode. Side effects of fenylefrine are rare (<0,01%) and consist of a allergic conjunctivitis, tearing, blurring of vision, prickling feeling, glaucoma, headache, subarachnoid haemorrhage, high blood pressure, tachycardia, arrhythmia, myocardial infarction.
After 10 minutes mydriasis will be achieved and subjects will undergo the slit lamp examination. For this the subject will have to sit in a chair, rest their chin on a holder and look straight ahead. The examiner, an ophtalmologic resident, will look with a bright light in the subject eyes. Additionally fundoscopie will take place. The subject keeps seated and will be asked to look straight ahead again. The examiner will look in the subjects eyes with the slit lamp and a special lens. During these tests there will be no direct contact with the eyes of the subjects and these tests bare no harm to subjects. However, the mydriasis with concomitant blurring of vision caused by the eye drops, may last for four to eight hours (followed by complete recovery). Therefore we advise subjects to arrange someone to take them home after the study visit. The ophthalomologic tests wilt take 70 minutes in total an the total study protocol takes one hour and 40 minutes.
If during neurological and/or ophthalmologic examination any symptoms that require further investigation or treatment are discovered, the participant will be informed and will receive a referral letter with our findings for his or her general practitioner.

Contacts

Public
Vrije Universiteit Medisch Centrum

De Boelelaan 1117
Amsterdam 1081 HV
NL
Scientific
Vrije Universiteit Medisch Centrum

De Boelelaan 1117

Amsterdam 1081 HV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

In order to be eligible to participate in this study, a patient must meet all of the following criteria:
- Clinical diagnosis of PD fulfilling the criteria of the UK PD Brain Bank (METC protocol, appendix B)
- (modified) Hoehn and Yahr stage 2 - 4 (METC protocol, appendix C) and a follow up of at least three years after diagnosis of PD.
- Age 50 - 70 years
- Best-corrected vision 20/30 or higher (using a Snellen chart)
- Intra-ocular pressure < 21 mmHg to rule out glaucoma;In order to be eligible to participate in this study, a control subject must meet all of the following criteria:
- Best-corrected vision 20/30 or higher (using a Snellen chart)
- Intra-ocular pressure < 21 mmHg to rule out glaucoma

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Media opacifications
- Concomitant ocular disease (glaucoma, retinal pathology, or pathology of the cornea, lens or optic nerve)
- History of ocular trauma
- History of laser therapy
- Degenerative neurological disease other than PD.
- MMSE < 26 in healthy controls (this is a possible indication of a degenerative neurological

disease)
- First degree relative with PD

Study design

Design

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

Primary purpose: Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-12-2014
Enrollment:	100
Type:	Actual

Medical products/devices used

Generic name:	Snellen chart;ocular pressure measurement device;slit lamp;fundoscopy and OCT machine
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	13-10-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-05-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	04-07-2017
Application type:	Amendment
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

ID: 29318
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL47617.029.14
OMON	NL-OMON29318