Functional Determinants of Parkinson*s Bradykinesia; A Kinematic, Neurophysiological and Psychophysical Study

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Primary Objective: 1. Test whether the flash lag illusion is decreased in PD and more specifically whether the decrease is associated with bradykinesia.Secondary Objective(s): 2. Quantify bradykinesia by means of motion sensors and validate this...

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

Summary

ID

NL-OMON38838

Source
ToetsingOnline

Brief title
Bradykinesia

Condition

- Movement disorders (incl parkinsonism)

Synonym
morbus Parkinson, 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

Intervention

Keyword: bradykinesie, Parkinson's disease, temporal processing, timing

Outcome measures

Primary outcome

4.5.1 Main study parameter/endpoint

Relation between:

* Duration of the flash lag illusion

* Score on bradykinetic UPDRS III items

* Movement amplitude, number of movements per second, acceleration and velocity

of hand, finger and foot movements

* Score on BRAIN test

Secondary outcome

4.5.2 Secondary study parameters/endpoints

Relation between:

* Movement amplitude, number of movements per second, acceleration and velocity

of hand, finger and foot movements

* Score on BRAIN test

* Score on bradykinetic UPDRS III items

* Subjective bradykinesia rating (1-10)

1. at end of dose interval

2. at beginning of dose interval

4.5.3 Other study parameters

Relation between:

* Dominant frequency of EEG background rhythm.

* Duration of the flash lag illusion.

* Score on bradykinetic UPDRS III items.

Study description

Background summary

Parkinson*s Disease (PD) is a neurodegenerative disorder with a clinical hallmark consisting of tremor, rigidity, postural instability and bradykinesia. Besides the prominent motor symptoms, also non-motor symptoms, including sensory processing and sensorimotor integration, are affected in PD. In this respect, PD symptoms may not only be due to impaired motor or sensory processing but may be a consequence of intrinsically disturbed sensorimotor integration. With regard to actions in external space, especially visuomotor integration is important.

Visuomotor integration includes the temporal adjustment of movements to sensory events. Our previous functional Magnetic Resonance Imaging (fMRI) experiment showed a crucial role for the Basal Ganglia (BG) in the temporal processing of velocity estimation. Further evidence for basal ganglia involvement in velocity estimation came from a subsequent behavioural experiment in which PD patients showed a selective disturbance in velocity estimation of a moving object seen on a screen. In our last experiment, we found that the severity of bradykinesia correlated with the magnitude of perceived accelerations. In the present experiment this latter issue will be further studied.

More specifically, in our previous experiment the degree to which a deceleration of the observed ball was judged as accelerating negatively correlated with the degree of bradykinesia, i.e. the judgment of the more bradykinetic patients was actually closer to the physical reality than that of the less bradykinetic patients. An explanation for this *acceleration bias* might be that *real-time* motor control requires feed-forward based processing to overcome intrinsic cerebral processing speed limitations. Such acceleration bias appears to be consistent with the *flash-lag* illusion in which the position of a moving stimulus is projected ahead compared to a stationary landmark. Up to now, no unifying neural mechanism underlying the flash-lag illusion has been postulated. However, a recent study indicated that TMS of area MT+, and not V1/2, reduced the perceived flash lag illusion. Interestingly, in a recent fMRI study by our group, area MT+ appeared to show

specific disturbances in visual motion processing in PD.

In accordance with the flash-lag illusion the functional basis of bradykinesia not fully elucidated either. One hypothesis is that the dopamine depleted BG fail to reinforce cortical mechanisms that prepare and execute commands to move. This might be due to pathological synchronisation in the BG, more specifically the subthalamic nucleus (STN). In one study, 20 Hz stimulation of the STN turned out to specifically increase bradykinesia in one study but not in a subsequent study.

Next to these deviant sub-cortical oscillations in bradykinesia, less is known about cortical oscillations (assessed with EEG) in PD*s bradykinesia. Despite sporadic reports, it was assumed until recently that non-demented PD patients do not show slowing of occipital background activity. However, recent evidence showed diffuse EEG slowing in PD patients without remarkable dementia. Regarding bradykinesia, one study reported a statistically significant association between the degree of motor disability and the dominant frequency of occipital background activity in PD patients without remarkable dementia. However, this study didn*t specifically look at bradykinesia per se. Although there is a lack of knowledge on the frequency of background activity in bradykinetic patients, attenuation of background activity during movements does correlate negatively with bradykinesia.

Bradykinesia is clinically tested by assessment of the bradykinesia items of the Unified Parkinson*s Disease Rating Scale (UPDRS). However, these items have the lowest reliability among all UPDRS items. For this reason, more quantitative measures using motion sensors are currently developed but not validated yet.

Study objective

Primary Objective:

1. Test whether the flash lag illusion is decreased in PD and more specifically whether the decrease is associated with bradykinesia.

Secondary Objective(s):

2. Quantify bradykinesia by means of motion sensors and validate this quantitative measurement by clinical bradykinesia judgement by a movement disorders specialist.
3. Correlating quantitative and qualitative bradykinesia scores with the dominant EEG background frequency.

Study design

A prospective cohort study will be conducted at the department of neurology of the University Medical Center Groningen.
For the experiment subjects will come to the outpatient department and will successively undergo:

1. A brief neurological examination (the UPDRS III) in which characteristic PD motor features will be investigated. Patients will be videoed during the examination and movement sensors will be attached on the relevant body parts.
2. A keyboard task quantifying bradykinesia (the BRAIN task [20] lasting approximately 5 minutes), will be conducted.
3. A subjective rating (1-10) to which degree patients experience bradykinesia will be obtained.
4. A psychophysical experiment in which subjects have to judge whether a moving ball stops simultaneously with a flash or not. This experiment presented on a laptop and responses will be given using a mouse. The task will last approximately 35 minutes consisting of 3 runs of 8 minutes with pauses of 5 minutes.
5. A 5 minute EEG registration in laying position with eyes closed will be conducted.
6. A brief cognitive screening task, the SCOPA-COG [21] will be performed.
7. Items 1 -3 will be repeated.

- patients will be planned to be tested at the end of their regular dose of Parkinsonian medication
- after item 2 of the experiment, patients will take their medication
- control subjects will only undergo steps 1, 2 and 5

Study burden and risks

There are no risks involved for the participating patients and controls. The experiment will require approximately 2 hours of the patients time in which the subjects will conduct a behavioural experiment, undergo a brief neurological examination and EEG and fill in a short cognitive task. There are no potential benefits for the participating patients.

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

Parkinson's disease

Exclusion criteria

tremor dominance
cognitive dysfunction
interfering neurological, ophthalmological, psychiatric or musculoskeletal disease

Study design

Design

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

Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-11-2013
Enrollment:	35
Type:	Actual

Ethics review

Approved WMO

Date:	13-11-2013
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
CCMO	NL45624.042.13