Feeling the beat: The neurophysiology of cueing in Parkinson's disease

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

Summary

ID

NL-OMON35309

Source
ToetsingOnline

Brief title
Neurophysiology of cueing in PD

Condition

- Movement disorders (incl parkinsonism)

Synonym
Parkinson's disease

Research involving
Human

Sponsors and support

Primary sponsor: Neurologie
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Freezing, Neural oscillations, Parkinson's disease, Rhythmic cueing

Outcome measures

Primary outcome

Behavioural performance is analysed in terms of reaction times.

Brain activity measured with magnetoencephalography (MEG) is analysed in terms

of its oscillatory patterns:

(i) presence and magnitude (power) of slow oscillations (< 1 Hz)

(ii) entrainment (i.e. phase synchronisation) of slow oscillations to external

cues

(iii) cross-frequency coupling of fast oscillations to slow oscillations

(iv) scalp distributions of these (the above) effects

Secondary outcome

not applicable

Study description

Background summary

The proposed research addresses an emerging paradox in current views on parkinsonian motor impairments. The paradox is that, on the one hand, it is believed that movements guided by external cues are relatively preserved in Parkinson*s disease (PD), providing a basis for the use of (rhythmic) cueing in rehabilitation. On the other hand, there is growing evidence that PD patients are not sensitive to temporal regularities in the environment and even have difficulty perceiving such regularities. We will address this paradox in an investigation into the neurophysiological basis of cueing. This may lead to differently targeted or more selective use of cueing strategies.

We will investigate the neurophysiological basis of cueing in PD by examining how patients differ from controls in spontaneous entrainment to environmental

regularities. Entrainment will be measured by means of slow brain oscillations recorded with magnetoencephalography (MEG). According to recent neurophysiological work in primates, endogenous slow brain oscillations spontaneously adjust their phase and frequency to temporally regular environmental events. The entrainment of slow oscillations, and nested faster rhythms, enables sensory brain structures to optimise perceptual processing and motor areas to adopt a predictive mode of control. We predict that the normal pattern of entrainment is defective in patients with PD.

We already have evidence that slow preparatory brain potentials are abnormal in PD, but do not know (i) whether this is due to lack of entrainment of slow endogenous oscillations, (ii) whether nested faster rhythms are similarly affected, and (iii) whether such abnormal oscillatory (re)activity contributes to motor impairments and insensitivity to environmental regularities. These questions are investigated in a series of experiments comparing PD patients with healthy controls. The experiments will manipulate environmental regularities in terms of relevance to task performance and by means of perturbations. The results will be vital to assess the potential of cueing strategies for rehabilitation, but are equally important to concepts of basal ganglia function and the role of abnormal oscillatory synchronization in the pathophysiology of Parkinson's disease.

Study objective

Key hypothesis of the investigation is that Parkinson*s disease is characterized by deficient entrainment of slow brain oscillations. Our previous work already provides preliminary support for this hypothesis. In order to evaluate to what extent this deficient entrainment limits the potential for cueing strategies, and can be remediated or circumvented in the rehabilitation of Parkinson patients, our objectives are to answer the following questions:
(i) Is deficient entrainment of slow brain oscillations due to abnormal entrainment or due to defective generation of slow brain activity?
(ii) Does abnormal generation or deficient entrainment of slow oscillations to regular environmental events carry over to nested faster oscillations associated with the processing of and motor responses to those events?
(iii) Does such abnormal oscillatory (re)activity contribute to motor impairments and insensitivity to environmental regularities?
(iv) What are the prospects of modifying the cueing approach such that, in spite of reduced spontaneous entrainment, cues can be used to advantage?

Study design

Observational research. The study consists of 5 separate experiments:

Experiment 1: Spontaneous entrainment of slow brain oscillations to rhythmic events

Experiment 2: Uncoupling of slow oscillations and faster rhythms
Experiment 3: Selective entrainment in the face of competing streams of rhythmic events
Experiment 4: Oscillatory entrainment and instructed use of rhythmic event structure
Experiment 5: Temporal coupling of deliberation and movement execution

Study burden and risks

There are no risks associated with the MEG measurements. Time burden is ~2 hrs for the actual experiment (including preparation and debriefing), plus an additional 0.5 hr for an head MRI scan if that has not been performed earlier (for research or clinical purposes).

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

- Idiopathic Parkinson's disease
- Age between 45 -70 years
- Moderate disease severity (Hoehn-Yahr 2-3)

Exclusion criteria

- Significant tremor (sustained and/or of high amplitude)
- Other neurological or psychiatric conditions, including stroke, traumatic brain injury, epilepsy, depression or anxiety disorder
- Significant cardiovascular risk factors (atherosclerosis, hypertension, hypercholesterolaemia, diabetes mellitus)
- Metal or electronic equipment implanted
- Severe visual impairment
- Declining to be informed of medically relevant chance findings in the investigation

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:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-12-2011
Enrollment:	150
Type:	Actual

Ethics review

Approved WMO Date:	08-11-2011
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL37859.091.11