Connections between the frontal lobe and the basal ganglia: possible biomarkers for dopaminergic deviations

Published: 20-09-2012
Last updated: 26-04-2024

The objective of this study is to determine the role of dopaminergic neurotransmission in the basal ganglia in response regulation.The outcome of the proposed studies is intended as proof of concept for our future research initiatives on the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON37920

Source
ToetsingOnline

Brief title
Networks of response selection

Condition

- Other condition

Synonym
none

Health condition

geen

Research involving

Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: fMRI, MRS, Saccade, TMS

Outcome measures

Primary outcome

Four different measures reflecting our control over automatic reactions will be obtained during 4 visits:

1. striatal dopime levels inferred from lactate content using 1H-MRS
2. functional MRI activation measurements in several regions of interest (ROI)
3. effect of TMS on frontal cortex on oculomotor control
4. average score per participant on several behavioral tests

A correlation analysis will determine whether inferred striatal dopamine levels per participant will correlate with measures 2-4. This outcome indicates whether striatal dopamine levels explain executive functioning and recruitment of areas in circuits involving the basal ganglia. When this is the case, the above measures are likely biomarkers for diseases affecting dopaminergic neurotransmission.

Secondary outcome

Not applicable

Study description

Background summary

The frontal cortex plays an important role in imposing higher order volitional control over automatic behavior. This allows us to react appropriately in complex and dynamic environments. The frontal cortex involvement in higher order control is eminent in response selection and motor control, but is suspected to extend to decision making, cognition, language and reasoning.
For some time, connections from the frontal cortex to the basal ganglia, and especially dopaminergic signaling therein, have been implicated in human response selection and decision making, although most of our knowledge about this system arises from work on animals. More recently, connections between the frontal cortex and the cerebellum have been implicated in our control over and learning of complex motor tasks.
Many neuropsychiatric diseases can be explained by defects in the aforementioned networks, but the exact neuropathology remains poorly understood. Response selection deficits occurring in schizophrenia, Parkinson's and Huntington's disease have all been explained by corroborated neuronal signaling in these networks, especially regarding dopaminergic metabolism in the basal ganglia, but this has hardly been investigated directly in human subjects. The present research proposal describes 2 experiments that investigate the function of (parts of) these two networks in healthy individuals. The techniques that are used are Transcranial Magnetic Stimulation (TMS), functional MRI (fMRI) and 1-proton spectroscopy (1H-MRS).

Study objective

The objective of this study is to determine the role of dopaminergic neurotransmission in the basal ganglia in response regulation.
The outcome of the proposed studies is intended as proof of concept for our future research initiatives on the dysfunction of the aformentioned networks in neuropsychiatric patients using the same techniques. Especially, using 1H-MRS as a technique to determine dopaminergic signaling deviations in the basal ganglia and their influence on response regulation might be tested as a disease biomarker.

Study design

This study investigates the role of fronto-basal connections in human response selection.

The study will measure functional properties of the human fronto-basal network in 4 visits by 40 healthy volunteers: 1) by determining the dopamine content in the human striatum through lactate 1H-MRS; 1) by investigating activity in this

network using fMRI during simple response selection tasks (eye movements); 3) by examining behavioral consequences of stimulating parts of this network with TMS; and 4) by measuring response selection and decision making, functions purported to be mediated by fronto-basal networks, using a series of behavioral paradigms. Correlations amongst these four measures will be examined within individuals. For example, will participants with low striatal dopamine levels be more reflexive and automatic in their behavior and will this also be reflected in reduced striatal fMRI activity? This series of experiments will also provide insight into the normal range of fronto-basal functioning, to provide a reference for examining dopaminergic dysregulation in psychiatric and neurological populations with basal ganglia dysfunction, such as Parkinson's and Huntington's disease, and schizophrenia.

The experiments are described in detail in chapter 5 (methods) of the protocol text.

Study burden and risks

The risk and burden associated with participating in an MRI, fMRI or TMS experiment is negligible, and are routinely performed in our institute. For potential risks of fMRI and TMS, the usual precautions are taken (proper screening, see D5).

Contacts

Public
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
3584 CX Utrecht
NL
Scientific
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
3584 CX Utrecht
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy subjects between age 18-50 years of age.

Exclusion criteria

The following list of exclusion criteria is used:
- nonremovable metal objects in head/body
- pregnancy
- history of closed or open head injury
- history of psychiatric illness
- history of neurological illness or endocrinological dysfunction
- history of epilepsy
- occurrence of epilepsy in 1st degree family
- use of medication other than anticonceptive or paracetamol
- drug or alcohol abuse over a period of six months prior to the experiment
-
intake of alcohol, caffeine or nicotine containing products within 4 hrs prior to the scanning s essions.
- claustrofobia

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-11-2012
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	20-09-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL39944.041.12