Dopamine-*-hydroxylase deficiency and cognitive function

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Ethical review	Approved WMO
Status	Pending
Health condition type	Neurological disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON29739

Source
ToetsingOnline

Brief title
Dopamine-*-hydroxylase deficiency and cognitive function

Condition

- Neurological disorders congenital

Synonym
Dopamine-beta-hydroxylase deficiency and cognitive function

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cognition, D□H deficiency, Norepinephrine

Outcome measures

Primary outcome

n/a

Secondary outcome

n/a

Study description

Background summary

In recent years, cognitive neuroscientists have become increasingly interested in understanding the role in cognition of the locus coeruleus-norepinephrine neuromodulatory system (i.e., the noradrenergic system). One way of investigating the noradrenergic system in humans is by examining cognitive abilities in patients with abnormal noradrenergic function. A particularly interesting group in this regard are patients with dopamine-*-hydroxylase (D*H) deficiency. This is a rare genetic syndrome that is characterized by a complete lack of norepinephrine, due to the congenital absence of the enzyme D*H. This enzyme is responsible for the conversion of dopamine into norepinephrine and in view of the total absence of this enzyme, patients with this syndrome are unable to synthesize any norepinephrine from dopamine. In this study, we will test some of these patients on a battery of cognitive tasks that have been proposed to depend on normal noradrenergic function. In addition, EEG and MRI data will be collected. The patients will be tested ON and OFF medication, on separate occasions. The results will be highly informative about cognitive function in D*H deficiency, and, more in general, about the role of the noradrenergic system in cognition.

Study objective

The main objective is to understand the role of the noradrenergic system in human cognition by testing specific hypotheses about task performance in D*H patients. A secondary objective is to understand whether and how cognitive function is compromised in D*H deficiency.

Study design

The study uses a quasi-experimental design. Patients will be tested ON and OFF medication, on separate occasions. A matched healthy control group will also be tested twice, in order to establish normal performance scores, and practice effects across the two test sessions.

Study burden and risks

Risk of non-invasive measurements: The risks associated with the cognitive tasks and EEG recording procedures are negligible. There are also no known risks associated with MRI. This is a noninvasive technique involving no catheterizations or introduction of exogenous tracers. Some people become claustrophobic while inside the magnet and in these cases the study will be terminated immediately at the subject's request. The only absolute contraindications to MRI studies are the presence of intracranial or intraocular metal, or a pacemaker. Relative contraindications include pregnancy and claustrophobia. Subjects who may be pregnant, who may have metallic foreign bodies in the eyes or head, or who have cardiac pacemakers will be excluded because of potential contraindications of MRI in such subjects.
Burden of invasive measurements: The only invasive procedure will be venapuncture. This has the usual risk of discomfort upon insertion of the needle and of hematoma.
Risk of stopping medication: stopping L-DOPS will cause levels of norepinephrine to fall to non-measurable low values. A gradual recurrence of orthostatic symptoms (fatigue and vertigo) will follow, In our experience this develops only slowly. Patients recognize these symptoms well, given that they have lived into adulthood without effective treatment. With proper instructions, probably self-evident for these patients, orthostasis will not be dangerous or detrimental in any way.

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

Patient group:
Patients with DßH deficiency
Control group:
Adult, healty volunteers with no history of neurological disorder/disease.

Exclusion criteria

none, all DBH patients in The Netherlands match the criteria for participation

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2007
Enrollment:	16
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL13544.058.06