GENETIC DETERMINANTS OF MONOAMINE METABOLITE LEVELS IN HUMAN CEREBROSPINAL FLUID

Published: 22-07-2008
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Identification of genetic variations that control monoamine and amino acid metabolism in humans, by translating recent genetic findings in non-human primates to a human cohort.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Mood disorders and disturbances NEC
Study type	Observational non invasive

Summary

ID

NL-OMON38098

Source
ToetsingOnline

Brief title
GDMA

Condition

- Mood disorders and disturbances NEC

Synonym
major depression; sadness

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: cerebrospinal fluid, gene, monoamine, psychiatry

Outcome measures

Primary outcome

Levels of HVA, 5-HIAA and MHPG in CSF will be tested for association with a set of single nucleotide polymorphisms (SNPs). The DNA region of interest is the chromosome region that is homologous to the region that was recently found to be linked with MAM levels in vervet monkeys. Once identified, the effect of associated polymorphisms on RNA expression of monoamine genes will be investigated. MAM levels and associated genotypes will be related to specific behavioral traits, as assessed through validated questionnaires.

Secondary outcome

As a secondary parameter, we will measure CSF amino acid concentrations and correlate these quantitatively to candidate genotypes and behavioral traits as assessed with the abovementioned questionnaires.

Study description

Background summary

Signaling mediated by monoamines (MA) -such as the neurotransmitters serotonin (5-HT), norepinephrine (NE) and dopamine (DA)- is thought to be compromised in many psychiatric disorders. Knowledge of the mechanisms that determine the levels of monoamines in the brain could increase our insight into the pathophysiology of many psychiatric diseases, which in turn could be helpful in developing new effective treatments. The turnover of DA, 5-HT and NE in the brain may be estimated by measuring their respective metabolites homovanillic acid (HVA), 5-hydroxyindoleacetic acid (5-HIAA) and 3-methoxy-4-hyrdoxy-phenylethyleneglycol (MHPG) in cerebrospinal fluid (CSF). Previous research has shown monoamine metabolites (MAM) in CSF to be party

under influence of genetic factors (Jönsson et al 2004). A recent quantitative trait locus (QTL) study of MAM concentrations in the CSF of vervet monkeys found genetic linkage on chromosome 9, which is homologous to human chromosome 10 (Freimer et al 2007).
In addition, previous research has shown that CSF amino acid (such as glutamate, glycine and aspartate) concentrations is aberrant in depression (Frye et al 2007).

Study objective

Identification of genetic variations that control monoamine and amino acid metabolism in humans, by translating recent genetic findings in non-human primates to a human cohort.

Study design

This study will be a cross-sectional, naturalistic study.

Study burden and risks

Spinal and venous canules are routinely inserted as part of the surgical procedure. The study will involve the collection and analysis of small amounts of CSF and venous blood through these existing lines, which does not constitute an additional risk. Phenotyping will require that subjects fill out online questionnaires (40-45 minutes) at a time that is convenient for them.

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

Military personnel and civilians referred for surgical procedures under spinal anesthesia whose four grandparents were born in The Netherlands will be included.

Exclusion criteria

Exclusion criteria are: age < 18 and > 58 years old and the use of benzodiazepines shortly before entering the operating theatre.

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-08-2008

Enrollment:	1000
Type:	Actual

Ethics review

Approved WMO Date:	22-07-2008
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	11-11-2008
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-06-2009
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-08-2010
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-01-2011
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-11-2012
Application type:	Amendment
Review commission:	METC NedMec

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	NL23042.041.08