Hersenvocht bij psychiatrische aandoeningen

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON26758

Source
Nationaal Trial Register

Brief title
CSF_PSYCH

Health condition

Psychosis, schizophrenia, affective disorders, depression

Sponsors and support

Primary sponsor: University Medical Center Utrecht
Source(s) of monetary or material Support: University Medical Center Utrecht

Intervention

Outcome measures

Primary outcome

CSF constituents:

- Autoantibodies to CNS receptors.

- A panel of cytokine, chemokine and growth factor levels.

- MiRNA levels.

- Neurotransmitter concentrations (including GABA, glutamate and all major amino acids).

- Plasma: Plasma levels of the CSF constituents mentioned under primary parameters.

- Genetic assessments: To unravel the contribution of genetic variation to the quantitative phenotypes under investigation here, and thereby potentially aid in the identification of genetic variation underlying psychosis, a hypothesis-driven genetic approach will be adopted.

-To link biochemical and genetic data to the behavioral level, we will have participants fill out questionnaires assessing a range of behavioral traits, as mentioned below.

Secondary outcome

- Plasma: Plasma levels of the CSF constituents mentioned under primary parameters.

- Genetic assessments: To unravel the contribution of genetic variation to the quantitative phenotypes under investigation here, and thereby potentially aid in the identification of genetic variation underlying psychosis, a hypothesis-driven genetic approach will be adopted.

-To link biochemical and genetic data to the behavioral level, we will have participants fill out questionnaires assessing a range of behavioral traits, as mentioned below.

Study description

Background summary

Rationale

Psychotic disorders, such as schizophrenia, depression with psychotic features and bipolar disorder, are prevalent disorders with far-reaching detrimental effects on mental wellbeing and psychosocial functioning. Treatment is still symptomatic due to the fact that the pathogenesis of these conditions is poorly understood. Being part of the central nervous system (CNS), cerebrospinal fluid (CSF) is the body fluid in closest proximity to the brain. Recent CSF studies in healthy subjects have proven highly informative for a range of biological and behavioral measures. However, sufficiently powered studies targeting CSF constituents in psychotic disorders are currently lacking. This protocol aims to assess CSF constituents in psychotic disorders to elucidate neurochemical, immunological, and metabolic processes underlying psychotic disorders.

Objectives

Primary objectives

- To investigate CSF autoantibodies (NMDAR, AMPAR, VGKC, and GABA receptors) in patients with a psychotic disorder and healthy controls.

- To compare levels of immune parameters between patients with a psychotic disorder and healthy controls.

- To compare neurotransmitter levels in CSF between patients with a psychotic disorder and healthy controls.

- To compare microRNA (miRNA) levels in CSF between these patients and healthy controls.

Secondary objectives

- To correlate CSF levels of the constituents mentioned under the first primary objective with peripheral plasma levels.

- To unravel the contribution of genetic variation to the variation in the primary outcomes.

- To relate temporal changes in CSF constituents to clinical outcome, i.e. improvement in symptoms.

- To assess how specific the detected differences in these constituents are for psychotic disorders.

Study design

Case-control study in patients with a psychotic disorder. The comparison groups are patients with affective disorders and a group of healthy individuals.

Study population

300 patients with a psychotic disorder (age > 18 years), 200 subjects with a non-psychotic affective disorder and 500 healthy individuals (age > 18 years).

Interventions

The participants will undergo two lumbar punctures (LP) and two venipunctures. The second

LP and venipuncture will take place between 4-12 weeks after the first. All subjects will additionally be asked to fill out questionnaires.

Main study parameters:

Primary parameters:

CSF constituents:

- Autoantibodies to CNS receptors.

- A panel of cytokine, chemokine and growth factor levels.

- MiRNA levels.

- Neurotransmitter concentrations (including GABA, glutamate and all major amino acids).

Secondary parameters:

- Plasma: Plasma levels of the CSF constituents mentioned under primary parameters.

- Genetic assessments: To unravel the contribution of genetic variation to the quantitative phenotypes under investigation here, and thereby potentially aid in the identification of genetic variation underlying psychosis, a hypothesis-driven genetic approach will be adopted.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness

This study does not include incapacitated subjects. Patients with psychotic or affective disorders will be given a compensation fee of €20 for their cooperation and time. In addition, possible travel costs will be reimbursed. Risks for participants are minimal. The most common adverse reaction to a lumbar puncture (LP) is post-puncture headache, transient nerve root irritation, lower back pain and a local hematoma (none of which jeopardizes patients' health). In the patient group we aim to minimize this risk by using an a-traumatic needle and applying standardized operating procedures (SOPs), including abiding by the UMCU LP protocol (see 'C1_Addendum_bij_Onderzoeksprotocol_Werkdocument Lumbaal punctie_herzien april 2015.pdf'), performance of LPs by experienced personnel and having the patient rest for at least 10 minutes prior to standing after the LP. Rare adverse reactions of LPs include hematoma (spinal, epidural, subdural or intracranial), infections (meningitis and discitis) and transient brain nerve damage. The prevalence of minor and transient neurological symptoms may be up to 15%, while the most serious adverse reaction (paraparesis) is not associated with LPs in patients who are not on anticoagulants during or shortly after the LP 1. Patients will be educated in detail about these possible adverse

reactions and as mentioned above we minimize these risks by abiding to evidence-based standards 2.

Healthy subjects will not be financially compensated. Our experience with these procedures in previous studies has shown that none of the >550 subjects included in these studies has suffered from adverse reactions to the lumbar punctures performed for these studies 3-7. These subjects undergo spinal anesthesia and a venipuncture for their minor surgical procedure, i.e. independent of the current study design. They thus do not undergo invasive procedures for the purpose of this study. Although suctioning of CSF in these individuals entails a longer LP duration (on average 30 seconds) compared to when they do not participate in the current project, no other types of burden are expected for these individuals.

There are no direct benefits for participants. In the future, patients may benefit from the current study in that treatment consisting of immunotherapy may be investigated for those patients with both psychosis and positive auto-antibody titers in their CSF. Moreover, possible aberrant neurotransmitter or miRNA profiles in their CSF may spur further research into treatment targets in psychosis.

Study objective

WE think we can find specific information about psychiatric disorder in the csf of psychiatric patients

Study design

At admission for patients and controls. Only a second time for patients

Intervention

Obtain CSF and questionnaires and blood

Contacts

Public
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Scientific
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Eligibility criteria

Inclusion criteria

Psychotic disorder patients: a DSM-IV or 5 classification of schizophrenia, schizophreniform disorder, schizoaffective disorder (both depressive and bipolar types), psychosis not otherwise specified (or other unspecified psychotic disorders), major depressive disorder with psychotic features, bipolar disorder with current psychotic features or a history of psychotic features and psychosis during the peripartum period (8 weeks after giving birth). DSM-IV or DSM-5 diagnosis will be clinician-rated or based on semi-structured interviews (i.e. the Semi-structured Clinician Interview for DSM Disorders, SCID).

Affective disorder patients: a DSM-IV or 5 classification of unipolar depressive or bipolar disorders without psychotic features. DSM-IV or DSM-5 diagnosis will be clinician-rated or based on semi-structured interviews (i.e. the Semi-structured Clinician Interview for DSM Disorders, SCID).

Healthy controls: participants in our previous study who consented to be contacted for future research purposes will be asked to fill out the one questionnaire that was not used in the previous study, the Youth Trauma Questionnaire (listed below). New healthy controls will be asked to fill out all questionnaires.
All participants: age > 18 years.

Exclusion criteria

Patients with psychotic or affective disorders
Subjects meeting any of the following criteria will be excluded from participation in this study:

-Lumbar-puncture specific (relative) contra-indications, again abiding by the UMCU protocol for LPs (see ‘C1_Addendum_bij_Onderzoeksprotocol_Werkdocument Lumbaal punctie_herzien april 2015.pdf’): a history of a severe adverse reaction to a previous lumbar puncture (reported by the subject and/or evident from the medical record, including post-puncture headache), the use of anticoagulant agents, thrombocytopenia, local infection of the skin, clinical signs of raised intracranial pressure or a suspected spinal epidural abscess.

- Although clotting abnormalities and suspected bacteraemia do not constitute contraindications for LPs, patients suffering from these will be excluded to avoid risks of excessive bleeding and infections.

- Patients who are not mentally competent and who don't have decisional capacity to decide about participation in this study will not be included. Doctors assess mental competence and decisional capacity of patients to ascertain whether they are able to express a choice,

understand and appreciate the information provided and reason about their possible participation. If there is any doubt about their mental competency or decisional capacity, the patient will not be included.

- Patients who were admitted to a psychiatric unit involuntarily after being given an ‘inbewaringstelling’ (IBS) will not be included. Patients with ‘rechterlijke machtigingen’ (RM) may be included, but only if they are mentally competent (see section on mental competence and decisional capacity above). The reasons for including the latter category of patients is that the inclusion of these patients will contribute to assembling a study population representative of all Dutch psychotic disorder patients.

- Some patients may participate in other studies as well. In those instances, the researchers of both studies discuss the option of simultaneous enrollment and decide about inclusion of the patient. Any decision about participation of patients in two studies will be based on balancing the advantages of dual study participation with the burden of such participation for participants.

Healthy controls

Subjects meeting any of the following criteria will be excluded from participation in this study:

- A current or past history of self-reported major psychiatric or neurological illness.

- Lumbar-puncture specific (relative) contra-indications: the anesthesiologist assesses these during routine pre-operative screening.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2017
Enrollment:	800
Type:	Anticipated

Ethics review

Not applicable
Application type: Not applicable

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
NTR-new	NL5763
NTR-old	NTR6005
Other	: ABRL 56840

Study results