Synaptic density in psychotic disorders

Gepubliceerd: 25-09-2019 Laatst bijgewerkt: 19-03-2025

Synaptic density as well as functional connectivity is expected to be decreased in patients with schizophrenia as compared to healthy controls. Functional connectivity and synaptic density in first-degree relatives is hypothesized to follow a…

Ethische beoordeling	Niet van toepassing
Status	Werving nog niet gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON27759

Bron
NTR

Verkorte titel
TBA

Aandoening

Schizophrenia, schizoaffective disorder, schizophreniform disorder

Ondersteuning

Primaire sponsor: Prof. Dr. I.E.C. Sommer
Overige ondersteuning: ZonMW

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

The main study parameter is the relationship between synaptic density and cognitive functioning and the potentially mediating role of functional connectivity in this relationship.

Toelichting onderzoek

Achtergrond van het onderzoek

Schizophrenia and related psychotic disorders (schizo-affective disorder and schizophreniform disorder) are severe mental disorders, placing a significant burden on global health. Patients suffer from a variety of psychotic, negative and cognitive symptoms. Additionally, they are at increased risk of developing metabolic syndrome and mortality with cardiovascular diseases is increased.
The genetic liability for psychotic disorders includes important loci in the human leukocyte antigen (HLA) area, which predisposes participants for increased and prolonged activation of microglia. Activated microglial cells have been reported to increase synaptic pruning in psychotic disorders, leaving the brain in suboptimal condition. The decreased synaptic density, resulting from accelerated pruning, is hypothesized to underlie cognitive dysfunction seen in the majority of patients with psychotic disorders. Potential ways how the loss of synaptic density may impair cognition is by affecting neuronal circuitry, which can be reflected in reduced functional connectivity as assessed with functional magnetic resonance imaging (fMRI). Although this theory has face-value, evidence to support it is currently absent, as studies invariably have either post-mortem material, which may evidence decreased synaptic density, or performance data on cognition and functional connectivity, but never the three together. Yet it is an important step to investigate whether and how decreased synaptic density in patients with psychotic disorders is the substrate of cognitive dysfunction and whether decreased functional connectivity is an intermediate step. It is now possible to measure these three variables: synaptic density, cognitive functioning and functional connectivity at the same time, since a new tracer has been developed to reflect synaptic density. [11C]-UCB-J((R)-1-((3-(11C-methyl-11C)pyridin-4-yl)methyl)-4-(3,4,5-trifluorophenyl)pyrrolidin-2-one) exhibits excellent Positron Emission Tomography (PET) tracer characteristics, including short-term test re-test repeatability and reproducibility across brain regions. This study will investigate if and how synaptic density may underlie cognitive deficits and whether functional connectivity is the intermediate step. In patients with psychotic disorders, cognitive functioning and brain connectivity may be decreased as a consequence of their genetic vulnerability. However, the use of anti-psychotic medication and lack of education, secondary to early disease onset may reinforce this effect. In an attempt to disentangle genetic vulnerability from secondary disease and medication effects, we also invite first-degree family members of the patients to participate.

Doel van het onderzoek

Synaptic density as well as functional connectivity is expected to be decreased in patients with schizophrenia as compared to healthy controls. Functional connectivity and synaptic density in first-degree relatives is hypothesized to follow a similar pattern as observed in schizophrenic patients, albeit abnormalities are anticipated to be less pronounced in first-degree relatives as compared to patients with schizophrenia.

Onderzoeksopzet

3

Onderzoeksproduct en/of interventie

N/A

Contactpersonen

Publiek

University Medical Center Groningen
Monique Germann

00491633347236

Wetenschappelijk

University Medical Center Groningen
Monique Germann

00491633347236

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. The participant understands the study and is able to provide written informed consent
2. Must be between the ages of 26-40
3. For patients: must have a diagnosis of schizophrenia, schizoaffective disorder, schizophreniform disorder
4. For siblings: must have 1 brother or sister with a disorders specified under point 3. The sibling is not necessarily related to one of the participants from the patient group.
5. For controls: participants must be free of any psychiatric or neurological disease and should not have any first- or second-degree relatives with one of the disorders specified under point 3.

Belangrijkste redenen om niet deel te kunnen nemen

(Exclusiecriteria)

1. Participation in a scientific research study during the past year involving radiation (or exposure to the same amount of ratiation within the past year via other means, e.g., transatlantic flights)
2. MR incompatible implants in the body
3. The possibility of having metal particles in the eyes
4. Tattoo’s containing red pigments that form a safety risk
5. Inability to undergo cognitive testing in Dutch
6. Dangerous or harmful behaviour (i.e. behaviour with a risk of severe physical injury, or actual physical injury inflicted, to self or others) occurred in last 3 months
7. Possibility of pregnancy
8. Intake of levetiracetam or brivaracetam

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Cross-over
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving nog niet gestart
(Verwachte) startdatum:	01-10-2019
Aantal proefpersonen:	78
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nog niet bepaald

Ethische beoordeling

Niet van toepassing

Soort: Niet van toepassing

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 49941
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL8046
CCMO	NL71100.042.19
OMON	NL-OMON49941

Resultaten