Effects of social exclusion on brain metabolism: a possible pathway for increased risk of schizophrenia in the hard of hearing.

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1. The baseline [123I]IBZM binding potential in the ventral striatum is higher among healthy subjects than among participants with acquired deafness (due to increased baseline activity of the mesolimbic dopamine system among participants with...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON23010

Bron
Nationaal Trial Register

Aandoening

schizophrenia, psychosis, sudden deafness, late deafness, dopamine, social exclusion

schizofrenie, psychose, plotsdoofheid, laatdoofheid, dopamine, sociale exclusie

Ondersteuning

Primaire sponsor: Academic Medical Centre, University of Amsterdam, the Netherlands
Overige ondersteuning: Academic Medical Centre, University of Amsterdam, the Netherlands

Rivierduinen, Leiden

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Decrease in [123I]IBZM-Binding Potential in the ventral striatum after amphetamine challenge.

Toelichting onderzoek

Achtergrond van het onderzoek

Background:

According to the social defeat hypothesis the long-term experience of social exclusion or social defeat leads to enhanced baseline activity and/or sensitization of the mesolimbic dopamine (DA) system and puts the individual at increased risk for psychotic disorder and/or schizophrenia. This pilot study tests the hypothesis by comparing DAergic function in two groups who are expected to differ greatly: (1) socially excluded young adults acquired deafness; (2) hearing peers.

Subjects and methods:

15 subjects with acquired deafness and 15 healthy subjects, recruited through patient organizations, treatment facilities and websites in the Netherlands, will be examined using SPECT-imaging with the D2 tracer [123I]iodobenzamide. In one session, baseline D2 receptor binding and endogenous DA release after stimulation with D-amphetamine sulphate (0.3 mg/kg iv) will be assessed (bolus/constant infusion technique). SAHI and healthy subjects will be matched for age, sex and smoking status.

Main hypotheses:

1. The baseline [123I]IBZM binding potential ([123I]IBZM-BP) in the ventral striatum is smaller in participants with acquired deafness than in hearing subjects, due to increased baseline activity of the mesolimbic dopamine system;

2. The decrease in [123I]IBZM-BP after amphetamine challenge is significantly greater in participants with acquired deafness than in hearing subjects;

3. There is a greater psychological/behavioural response to amphetamine (happiness, restlessness, increased level of energy) in subjects with acquired deafness than in hearing

subjects.

Power:

Animal experiments have demonstrated large effects of humiliation on DA function (Cohen’s d > 1), but there has not been any study in humans. It is proposed to compare 15 deaf subjects and 15 healthy subjects using a t-test for independent samples. Thus, the study has 85% power (α = 0.05; one-tailed) to demonstrate a large effect size (Cohen’s d = 1.0). The results will be examined for confounding and effect modification by socio-economic status, salivary cortisol, serum testosterone and polymorphisms of genes coding for COMT, DA transporter and D2-receptor.

Scientific and social relevance:

1. The social defeat hypothesis may explain the higher risk of major psychiatric disorder for people who rank low in societal hierarchy;

2. Understanding the biological mechanisms underlying the unequal risk is a first step towards prevention.

Doel van het onderzoek

1. The baseline [123I]IBZM binding potential in the ventral striatum is higher among healthy subjects than among participants with acquired deafness (due to increased baseline activity of the mesolimbic dopamine system among participants with acquired deafness);

2. The decrease in [123I]IBZM binding potential after amphetamine challenge (representing endogenous DA release) is significantly greater in participants with acquired deafness than in healthy subjects;

3. The [123I]IBZM binding potentials before and after amphetamine challenge are correlated with scores on scales related to social exclusion and self esteem (UCLS, Social Defeat Scale, Social Comparison Scale, BCSS, RSES);

4. There is a greater psychological/behavioral response to amphetamine (happiness, restlessness, increased level of energy) in participants with acquired deafness than in hearing control subjects;

5. The [123I]IBZM binding potentials before and after stimulation with amphetamine are correlated with scores for non-clinical psychotic or psychosis-like symptoms.

Onderzoeksopzet

Testing day 1:

1. Edinburgh Handedness Inventory;

2. Number of addresses in range of postal code, for three different time frames, current residence / longest residence age 0-10 yrs / longest residence age 10-20 yrs;

3. Parental Education levels;

5. Deaf participants: Audiogram. Control participants: Automated (Békésy) audiogram.

For deaf participants only:

4. Question about deafness in medical interview;

6. Speech audiometry.

Testing day 2 (preferably within 1 month of testing day 1):

7. UCLA Loneliness Scale (v3);

8. Social Defeat Scale;

9. Rosenberg Self Esteem Scale;

10. Beck Depression Inventory (II);

11. Social Comparison Scale;

12. Childhood Trauma Questionnaire;

13. Community Assessment of Psychic Experiences;

14. Visual Analogue Scale, t(amphetamine) -5, 5, 15, 25, 35, 45, 55, 120 minutes;

15. Community assessment of Psychic Experiences - state version. 2x. Assessing the 120 minutes before and 120 minutes after amphetamine administration;

16. Brief Core Schema Scales;

17. Cortisol from saliva, 2x. Directly before each SPECT scan;

18. Blood sample before start of IBZM infusion;

19. Blood sample before start of IBZM infusion;

20. Either 3t scan acquired locally, or for CI users scan acquired at institution where Cochlear Implant was placed;

21. SPECT Scan, 2x. 120 minutes after start of IBZM infusion and 240 minutes after start of IBZM infusion (60 minutes after D-amphetamine infusion);

22. Blood sample, 4x (directly before and after each SPECT scan);

23. Cognitive Emotion Regulation Questionnaire (CERQ);

24. Penn Emotion Recognition Task (PERT);

25. Hinting task;

26. Blood pressure measurements t(amphetamine) -5, 0, 5, 10, 15, 20, 25, 30 minutes.

Onderzoeksproduct en/of interventie

The procedure for deaf (n=15) and control (n=15) participants is the same. Participants with acquired deafness are assumed to have experienced extreme social exclusion due to their loss of hearing. Control participants will be matched to deaf participants on age (+/- 1 yr), sex, and smoking habits.

D-amphetamine sulphate iv (0.3 mg/kg body weight).

Contactpersonen

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Age 18-30 years;

2. Dutch ethnicity;

3. Participants with acquired deafness: Bilateral hearing loss of at least 60 dB (averaged over 500, 1000, 2000, 4000 Hz) present for at least 3 years. Hearing loss in the best ear was no more than 80 dB before age 2;

4. Control participants: Bilateral hearing loss of less than 20 dB (averaged over 500, 1000, 2000, 4000 Hz).

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Current or past psychotic disorder (according to CASH-interview);

2. Psychotic disorder in parents or full siblings (according to FIGS-interview);

3. Current or past use of illicit drugs (according to CASH-interview). A urine drug screen on cannabis, cocaine, amphetamines and opiates should be negative. A lifetime maximum of 10 cannabis consumptions is allowed. No consumption of cannabis during past year. Never any use of hard drugs;

4. Alcohol abuse/dependence or history of alcohol abuse/dependence (according to MINI-plus);

5. History of meningitis;

6. Neurological disorder (e.g., epilepsy) or evidence of brain damage (e.g., history of cerebral contusion. Cerebral concussion is not an exclusion criterion);

7. Current use of drugs known to interfere with IBZM binding to D2 receptors and/or DA release. Current or past use of antipsychotic drugs;

8. Failure to complete regular primary school;

9. Metal objects in or around body, with the exception of Cochlear Implants;

10. Control subjects: major impairments which may lead to social exclusion (e.g., dependence on wheel chair);

11.Participants with acquired deafness: no other major impairments than acquired deafness leading to social exclusion;

12. In women: pregnancy or lactation;

13. Participated in research with radiation exposure during the year preceding the study;

14. Clinical diagnosis of Attention Deficit Hyperactivity Disorder (ADHD);

15. Current major depressive disorder (single episode or recurrent, according to CASH-interview).

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Parallel
Toewijzing:	Niet-gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-10-2010
Aantal proefpersonen:	30
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	01-09-2010
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 32473
Bron: ToetsingOnline
Titel:

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL2385
NTR-old	NTR2492
CCMO	NL24257.018.08
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON32473

Resultaten

Samenvatting resultaten
N/A