A comparison of nigrostriatal dopaminergic functioning in healthy adults of West-African and European descent

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1. To examine whether there is an increase in (nigro)striatal dopaminergic functioning in individuals of West-African descent relative to those of Dutch descent (assessed in older participants with DAT SPECT and with NM-MRI in the entire sample). (…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Neurological disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON56593

Source
ToetsingOnline

Brief title
The relationship between ancestry and dopamine in the brain

Condition

- Neurological disorders NEC
- Schizophrenia and other psychotic disorders
- Economic and housing issues

Synonym
Alterations in the dopamine system relevant to Parkinson's disease & schizophrenia/psychosis

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: NWO Veni-beurs en overige beurzen van het Amsterdam UMC,Stichting J.M.C. Kapteinfonds

Intervention

Keyword: ancestry, Dopamine, NM-MRI, SPECT

Outcome measures

Primary outcome

(1) In older participants (>=50 years old) only: Striatal dopamine transporter (DAT) availability, as assessed through [123I]-FP-CIT SPECT by examining the specific striatal [123I]-FP-CIT binding.

(2) In all participants: Nigrostriatal dopaminergic functioning, as assessed with the neuromelanin-sensitive MRI (NM-MRI) contrast-to-noise ratio (CNR) in the substantia nigra.

These outcomes will be compared between participants of West-African and Dutch descent.

Secondary outcome

1. Subjective social status, i.e. the participant*s perceived standing (1) within Dutch society and (2) their community. This will be measured with the MacArthur Subjective Social Status Scale (MSSSS).

2. Scores on the Barratt Simplified Measure of Social Status (BSMSS), which reflects socioeconomic status (SES), i.e. the participant*s objective socioeconomic position in society, based on educational level and occupational status. Personal and household income will also be quantified.

These outcomes will be correlated with striatal dopaminergic functioning and

compared between West-African and Dutch participants.

Study description

Background summary

Compared to individuals of European descent, those of African descent show a greater risk of developing schizophrenia, but a lower risk of developing Parkinson's disease (PD). Schizophrenia is characterized by increased striatal dopaminergic functioning, whereas PD is the result of nigrostriatal dopamine degeneration. Investigating the neurobiological mechanisms underlying schizophrenia and PD can help explain racial disparities in disease risks. Specifically, we hypothesize that an upregulation in striatal dopaminergic functioning in African individuals relative to European individuals increases the risk of schizophrenia, but protects against PD. These striatal dopaminergic alterations might arise from genetic differences, but might also be linked to variations in social stress exposure (e.g., stress resulting from low status).

Study objective

1. To examine whether there is an increase in (nigro)striatal dopaminergic functioning in individuals of West-African descent relative to those of Dutch descent (assessed in older participants with DAT SPECT and with NM-MRI in the entire sample). (Primary objective)
2. To examine whether (nigro)striatal dopaminergic functioning is in both racial groups negatively associated with measures of social status. (Secondary objective)

Study design

Cross-sectional.

Study burden and risks

Burden and risks:
The burden associated with this study is moderate, the risk is minimal. Subjects visit the Amsterdam UMC two or three times: for psychological assessments, an MRI-scan, and (older participants only) a SPECT scan (depending on the availability of the participant and the scanners, the MRI- and SPECT scans can sometimes be planned on the same day for older participants, in which case they will only have to visit two times). For the SPECT scan, participants will receive a dose of approximately 111 MBq [123I]-FP-CIT, which induces a radiation burden of approximately 2.7 mSv. In the Netherlands, the natural background activity per year is approximately 2.9 mSv, so the additional

radiation induced by participation in this study is similar to the amount of natural background activity detected in one year. A small amount of blood will also be taken from each participant. The methods applied in this study are part of routine clinical care and have been widely used in scientific studies worldwide and at the Amsterdam UMC.

Benefits:
There are no direct benefits to the participants. However, the study will contribute to our understanding of the aetiology of schizophrenia and PD. The first step towards prevention is understanding the biological mechanisms. Thus far, individuals of African descent have been largely excluded from neuroimaging studies, which has resulted in a knowledge gap about their neurobiology and health. For the prevention of schizophrenia among people of African descent it is important to know whether there is an increase in nigrostriatal dopaminergic functioning. If so, it is vital to know whether the increase is due to genetic factors or low status. The findings on Africans may provide clues for prevention of PD, and directly inform clinical practice (e.g., by contributing to the calibration of DAT SPECT standards/reference data in different racial groups).

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

1. Age 18-70 years old.
2. West-African or Dutch descent, as determined through self-report (parents and grandparents should be born in the corresponding region). After the study has been conducted, ancestry will be confirmed with genetic analysis.
3. Speaks Dutch or English.

Exclusion criteria

1. Present or past (suspected) presence of severe psychiatric illness, such as schizophrenia or other psychotic disorder, bipolar disorder, depressive disorder with psychotic features.
2. Present or past (suspected) presence of neurological disorder (e.g., Parkinson*s disease, epilepsy), evidence of brain damage, and/or other medical illness (e.g., diabetes mellitus) that may affect brain function.
3. Current or recent (past three months) use of illicit drugs, as determined by self-report and with a urinary drug test on the day of neuroimaging (the results of this drug test will be checked after the participant has completed the study). Participants will be tested on use of cannabis, amphetamines, XTC, cocaine and opiates.
4. Lifetime use of illicit drugs (in particular opiates, amphetamines, XTC, and cocaine; exclusion for other illicit drug use will be decided on a case-by-case basis), if frequently taken (>10x lifetime use of drugs).
5. Lifetime cannabis use, if frequently taken (weekly use for at least a year).
6. Current or recent (past three months) use of dopamine-altering medications/drugs that might influence neuroimaging of DAT availability, namely: amphetamines, cannabis, cocaine, CNS stimulants phentermine or ephedrines, modafinil, certain antidepressants (mazindol, bupropion, radafaxine), adrenergic agonists, anticholinergic drugs, opioids, anesthetics ketamine, PCP, or isoflurane.
7. Smoking or consuming caffeinated drinks during the period of six hours prior to the DAT SPECT scan.
8. Participation in a scientific examination that used radiation, in the last year.
9. (Non-removable) metal objects in or around the body.
10. In women: pregnancy (self-report or positive pregnancy test) and/or

lactation.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-05-2024
Enrollment:	80
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	04-12-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-03-2024
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
Other	https://osf.io/697s2
CCMO	NL83230.018.22