Dopaminergic and noradrenergic dynamics after acute stress

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In this study, we aim to prove a double dissociation between the contribution of dopamine and norepinephrine during the acute stress response.

Ethical review	Approved WMO
Status	Completed
Health condition type	Anxiety disorders and symptoms
Study type	Interventional

Summary

ID

NL-OMON51949

Source
ToetsingOnline

Brief title
DANDYN

Condition

- Anxiety disorders and symptoms

Synonym
Anxiety disorders, Stress-related disorders

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: ERC grant

Intervention

Keyword: Dopamine, Noradrenaline, Stress

Outcome measures

Primary outcome

The main study parameters are the comparison of oddball performance and performance in the cue-guided versus memory-guided attention task, between the stress and placebo group, the stress and haloperidol group, and the stress and propranolol group.

Secondary outcome

In this study, three secondary outcome parameters are measured. First, the difference in vigilance and striatal-dependent cognition between the group receiving Propranolol and the group receiving Haloperidol is investigated.
Second, the difference in neural activity between the different groups is assessed during the oddball and visual search task.
Third, the difference in behavioral measures and neural activity in the different groups is measured during a motivation task, a working memory task, and an emotion task.

Study description

Background summary

A stressful event generates a cascade of bodily changes, enabling humans to best adapt to a potential threat. A variety of disorders are tied to a maladaptive response to a stressful event. Part of the normal stress response entails an enhancement of the production of catecholamines in humans, notably dopamine and norepinephrine. Although the increased production of these neurotransmitters to stress has been documented, the function of these catecholamines in the stress response are understudied. In this study, we hypothesize that dopamine inhibition decreases striatal-dependent function after acute stress, but not vigilance, while norepinephrine inhibition decreases vigilance after acute stress, but not striatal-dependent cognition. A

better understanding of the mechanism of these catecholamines might help to develop more effective treatment for patients with stress-related disorders.

Study objective

In this study, we aim to prove a double dissociation between the contribution of dopamine and norepinephrine during the acute stress response.

Study design

Our hypothesis will be tested in a double-blind, placebo-controlled, between subjects design.

Intervention

This study will investigate four groups. The first group receives the control procedure, while groups 2,3, and four undergo the stress procedure. Group 1 and 2 additionally receive two placebos. The third group receives 2 mg of Haloperidol as well as a placebo, while the fourth group receives 40 mg of Propranolol as well as a placebo.

Study burden and risks

Participants will come to the lab on two different occasions. Once for screening and a structural MRI session, and once for a functional MRI session. During the first session, participants will perform a questionnaire battery, as well as behavioral tasks. The days before the second session, participants are required to refrain from drug, smoking, and alcohol use. During the second session, participants will receive a drug or placebo. In order to make the intake of Haloperidol and Propranolol as safe as possible, a medical screening will be performed, and a MD will be present during the testing day. On the testing day, participants get the drug or placebo, as well as a stress induction test (the Socially Evaluated Cold Pressor Task). The participants will perform some tasks before entering the MRI, in the MRI, and after the MRI scan. Both Haloperidol and Propranolol are commonly administered, used for clinical use, and safe in these doses (40 mg and 2 mg single use respectively).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Age between 18 and 40
Right handed
BMI between 18.5 and 30
Normal or corrected to normal vision
Speaking and understanding of the English language

Exclusion criteria

Incompatibility with the MRI scanner
History of brain surgery
Possible pregnancy
Breastfeeding
Color blindness
Any relevant current or past psychiatric or psychotic disorder, including suicidality
First degree family member with schizophrenia, bipolar disorder, or major depressive disorder
Neurological disorder
Endocrine disorder
Endocrine treatment

Glaucoma or increased risk for glaucoma
Melanoma or undiagnosed skin lesion
Any other clinically significant hepatic, metabolic, obstructive respiratory, renal, cerebrovascular, cardiovascular, oncological, ocular or pulmonary disease/disorders
Raynaud*s syndrome
Hypersensitivity to Haloperidol or Propranolol
Hypertension (i.e. diastolic blood pressure >95 mmHg at rest, or systolic blood pressure >180
mmHg at rest)
Hypotension (i.e. diastolic blood pressure <50 mmHg at rest, or systolic blood pressure <95
mmHg at rest, or heart rate <45 bpm)
A-V block (PR interval longer than 0.20sec or irregular PR intervals)
Abnormal QTc-interval (higher than 450 for males, and 460 for females)
Frequent autonomic failure (fainting, dizziness, blurry vision)

Used prescribed medication within the last month
Use of *over the counter* medication within the last two months (excluding paracetamol)
Dependence on alcohol or drugs
Use of alcohol within 24 hours before the test sessions
Average alcohol consumption of 3 beverages or more daily
Use of drugs within 72 hours before the test sessions
Cannabis use within 2 weeks prior to start of the study, weekly use for a duration of at least 3
months in the last 6 months
Weekly or more use of recreational drugs or psychotropic medication
Habitual smoking (more than one pack in a week) or inability to cease smoking for 24 hours
before testing
Irregular sleep/wake rhythm
Intense daily physical exercise
Native English speaker

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial

Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	22-06-2022
Enrollment:	132
Type:	Actual

Ethics review

Approved WMO Date:	08-03-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-04-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-11-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-06-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL78603.091.21