NMDA-receptor blockage to Prevent Trauma Induced Symptomatology

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

Summary

ID

NL-OMON56481

Source
ToetsingOnline

Brief title
N-PTIS

Condition

- Anxiety disorders and symptoms

Synonym
anxiety disorder

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: ZonMwOffroad 04510012110026

Intervention

Keyword: Intrusions, NMDA receptor, Stress

Outcome measures

Primary outcome

The primary outcome is the number and distress of self-reported intrusive memories in the 7 days following the trauma-analogue . This will be analysed using a mixed negative binomial regression. *Participant* and Day (treated as continuous) will be random factors and treatment as fixed factor.

Secondary outcome

Three moderation analyses will be performed to test whether baseline brain derived neurotrophic factor (BDNF) levels, chronic stress and acute stress response moderate the effect of blocking NMDA-receptor on intrusive memories.

Study description

Background summary

Intrusive memories are common in the aftermath of psychological trauma. The number of intrusions experienced within days after traumatic events are associated with acute post-traumatic stress symptoms and predict the developoment of posttraumatic stress disorder (PTSD). Although there are widely implemented evidence-based treatments for PTSD, these methods focus on mitigating stress-related symptoms due to repeated and distressing memory intrusions over a longer period of time. In contrast, the field so far lacks interventions to hinder the initial build-up of intrusions.

Study objective

In this project, pharmacotherapy will be used to target the molecular basis of memory consolidation in the acute trauma phase to prevent the intrusive aspects of traumatic memories from forming. An excellent candidate to pharmacologically manipulate memory consolidation during the acute trauma phase is the N-methyl-D-aspartate (NMDA) receptor antagonist, esketamine. It is hypothesize

that blocking the NMDA-receptor with a low-dose esketamine will result in less intrusive memories when administered 1 hour after trauma during memory consolidation.

Study design

The study is a between-subjects design. Participants will receive the study medication using a nasal spray with either esketamine or the active-comparator (midazolam) one hour post viewing a car accident in virtual reality (VR). Participants will experience an incidence of stress induction before this.

Intervention

Participants receive 1x estketamine (28mg; 14mg per 100mL spray) or 1x the active-comparator (midazolam; 1.25mg per dosis).

Study burden and risks

Participants will complete mental health screening questionnaires, provide saliva samples (3 x sampling), a hair sample (1 sample), 1 blood sample (7.5ml) for BDNF analysis, blood pressure recordings (3 measurements), and measures of cognitive functioning. The second lab visit will consist of exposure to a stress manipulation followed by watching the VR car-accident scenario and taking the study treatment (esketamine or active-comparator). Intrusive memories will also be assessed outside the laboratory setting using the free smartphone app (https://m-path.io) during the subsequent 7 days. Participants will be invited for an online session one week and one month later to discuss diary compliance, to fill-out the impact of Event Scale to assess intrusion, avoidance, and hyperarousal as PTSD related symptoms. These one week and one month follow-up sessions are also to check how the participant is doing.

The stress manipulation has been shown to be well tolerated (ECP-77-3-01-2009-2). The VR scenario has been developed for educational purposes for young drivers by the Leicestershire Fire and Rescue Service. Most important additional precautions are: determining the absence any mental or physical disorder and use of any medication. In addition, esketamine and midazolam are well tolerated when taken 1x intranasal. If there are any side effects, these are mild and of short-lasting nature.

In case they experience medical complaints, the medical supervisor will be contacted. If participants feel discomfort after participating, they can contact an independent clinical psychiatrist (dr. Sjacko Sobczak).

Contacts

Public
Universiteit Maastricht

Universiteitssingel 40
Maastricht 6229 ER
NL
Scientific
Universiteit Maastricht

Universiteitssingel 40
Maastricht 6229 ER
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Written informed consent
• Good physical and mental health as determined by medical screening
• Age between 18 and 35
• BMI between 17.5 - 28
• A competent level of English to answer the questionnaires

Exclusion criteria

• Diagnosis of a psychiatric disorder (DSM-V)
• Use of any pharmacological treatment at time of inclusion
• Current recreational drug use/dependence
• Current alcohol dependence

• Pregnancy or plans to get pregnant in the near future;
• Hypertension (systolic BP >160 mm Hg or diastolic BP >90 mm Hg)
• Previous (recreational) use of PCP or ketamine.
• Heavy smoking (>10 cigarettes/week)
• Having experienced a car accident

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:	Recruiting
Start date (anticipated):	05-03-2024
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO

Date:	28-02-2024
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL85042.068.23