The role of anticipation in nocebo effects on pain

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Primary research question: Does the amplitude of late SPN in the 500ms preceding a pain stimulus differ between the anticipation of moderate pain versus heightened, nocebo augmented pain, during the evocation of nocebo effects on pain? Primary…

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON21903

Bron
NTR

Verkorte titel
TBA

Aandoening

Healthy participants

Ondersteuning

Primaire sponsor: Leiden University, Leiden, the Netherlands
Overige ondersteuning: NWO Vici Grant Number: 45316004

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

Stimulus preceding negativity (SPN) during evocation: The primary outcome of the study is the measurement of SPN, an event related potential (ERP) component used as a measure of

anticipatory processing. Late SPN, measured in the 500ms directly prior to the onset of the thermal pain stimuli, will be compared between control and nocebo evocation phase trials to measure whether learned nocebo effects correspond with changes in anticipatory processing prior to experiencing pain. The mean signal of all evocation phase trials free of artifacts in the EEG data from included participants will be included in this analysis.

Toelichting onderzoek

Achtergrond van het onderzoek

In this study on healthy adult participants, we will use electroencephalography (EEG) to measure neural activity during the anticipation of 'normal' and 'nocebo-augmented' pain. By exploring the differences in how the brain anticipates pain under these conditions, we aim to better understand how learned expectations shape painful experiences. Nocebo effects on thermal pain will be induced in a single group of 42 participants (sample size derived from a power analysis of Morton et al., 2010) using a verbal suggestion and classical conditioning paradigm while EEG is recorded.

Doel van het onderzoek

Primary research question: Does the amplitude of late SPN in the 500ms preceding a pain stimulus differ between the anticipation of moderate pain versus heightened, nocebo augmented pain, during the evocation of nocebo effects on pain?
Primary hypothesis: Late SPN amplitudes in response to cues (colored text on a computer screen indicating the activation of a (sham) TENS device), measured in the 500ms preceding cued stimuli, will be increased in anticipation of nocebo trials, as compared to control trials, in the evocation phase.
2. Secondary (exploratory) research questions and hypotheses:
2a. Research question: Does the amplitude of late SPN in the 500ms preceding a pain stimulus differentiate between the anticipation of moderate, control pain and heightened pain, during the acquisition of nocebo effects on pain?
Hypothesis: Late SPN in response to cues 500ms preceding nocebo and control pain stimuli, will be increased during nocebo trials, as compared to control trials, in the acquisition phase.
2b. Research question: Will differences in late SPN amplitude between the first half of nocebo and control evocation trials correlate with the magnitude of self-reported nocebo augmented pain (i.e., noceboe effect) for the evocation phase?
Hypothesis: The magnitude of late SPN (nocebo minus control amplitudes) will correlate with the magnitude of the nocebo effect.
2c. Research question: Does anticipatory neural processing measured with Granger Causality Analysis in the 1000ms preceding pain stimuli differ between moderate pain and heightened, nocebo augmented pain during the acquisition and evocation of nocebo effects?
Hypothesis: Anticipatory neural processing measured 1000ms prior to nocebo pain stimuli in frontal electrodes will predict neural activity in the following 1000ms in temporoparietal electrodes, from the onset of the pain stimulus, modelled with Granger Causality analysis.

This model will be compared to a model for control pain stimuli, separately for the acquisition and evocation phases.
2d. Research question: How does fear of pain relate to self-reported nocebo augmented pain during the first half of the evocation phase?

Hypothesis: Higher fear of pain will be correlated with higherself-reported nocebo augmented pain during the first half of the evocation phase. The analysis will be repeated with the entire evocation phase as an exploratory analysis.
2e. Research question: How does fear of pain relate to networks of anticipatory neural processing preceding nocebo-augmented pain during the evocation phase?
Hypothesis: Higher fear of pain will be correlated with a larger difference in SPN and Granger Causality values between? nocebo and control evocation phase trials.

Onderzoeksopzet

Participants complete the study in a single lab visit of approximately 2 hours in duration, during which the primary and secondary outcomes are measured.

Onderzoeksproduct en/of interventie

Verbal suggestions: Participants are told at the start of the experiment, and again just prior to the conditioning paradigm, that pulses from an electrical stimulation device attached to their aim via two electrodes will increase the intensity of the thermal pain stimuli when the electrical stimulation device is turned on.

Classical conditioning: Participants undergo a classical conditioning paradigm intended to form an association between the (sham) activation of the electrical stimulation device and increased pain intensity. The acquisition phase of the paradigm, during which time the association is learned, consists of 40 control and 40 reinforced nocebo pain stimuli trials. During control trials, a thermal stimulus calibrated to evoke moderate pain intensity (approximately 4 on a 0-10 pain scale) is paired with a message on a computer screen stating the electrical stimulation device is turned off. During reinforced trials, a thermal stimulus calibrated to evoke moderate pain intensity (approximately 7 on a 0-10 pain scale) is paired with a message on a computer screen stating the electrical stimulation device is turned on. The evocation phase of the paradigm, during which time the learned association is tested, consists of 30 control and 30 nocebo pain stimuli trials. These trials are identical to those of the acquisition phase with the distinction that now the pain stimuli for both trial types are set to the moderate pain intensity previously used only during control trials.

Contactpersonen

Publiek

Leiden University
Andrea Evers

+31 71 527 6891

Wetenschappelijk

Leiden University
Andrea Evers

+31 71 527 6891

Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

Adults ages 18-35
Strong understanding of written and spoken English
Normal or corrected to normal vision

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Ever having experienced serious medical or psychiatric conditions (e.g., heart or lung disease, panic attacks, alcohol addiction, clinical depression), including any present conditions thought to increase the risk of a serious COVID-19 infection (diabetes, severe obesity, HIV, severe kidney or liver diseases) and the presence of any condition or treatment that causes a reduced resistance to infections (autoimmune disorders, blood disorders, organ or stem cell transplant recipients, people without spleens).
2. Currently experiencing or having experienced in the last 48 hours any symptoms of COVID-19 (cough, sore throat, fever, trouble breathing, muscular pain, pain behind the eyes, excessive fatigue, diarrhoea, loss of sense of smell or taste).
3. Having tested positive for COVID-19 fewer than 7 days ago.
4. After testing positive for COVID-19 more than 7 days ago, not being symptom free for at least 48 hours.
5. Having a housemate/partner test positive for COVID-19 (or an untested but suspected COVID-19 infection) in the past month.
6. Ever having experienced chronic pain complaints (pain for more than 6 months).
7. Ever having experienced persisting painful health problems in the last 6 months.

8. Ever having experienced acute physical pain (more than 1 on the 0-10-point pain Numeric Rating Scale (NRS); e.g., mild headache), on the day of testing.
9. Having used pain medication or recreational drugs in the 24 hours prior to testing.
10. Having consumed more than 3 caffeinated drinks (coffee, tea, energy drinks, etc.) on the day of testing, any alcohol the day of testing, or more than 3 units of alcohol in the 24 hours before testing.
11. (Intended) pregnancy or breastfeeding.
12. Having recent injuries to the head, wrists or arms on the day of testing.
13. Previous participation in this or similar studies (e.g., using thermal pain).
14. On the day of testing: not being able to sufficiently distinguish between the different temperatures during calibrations and nocebo acquisition, or not reporting a pain of at least 6 (0-10 pain NRS scale) with the highest temperature used during calibrations.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Enkelblind
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	06-04-2021
Aantal proefpersonen:	42
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Ja

Toelichting
Coded, nonidentifiable, pseudoanonimized individual data relevant to all analyses reported in publications stemming from this project will be made available after the publication(s) are released. Data will be available upon request through an online database such as DataverseNL.

Ethische beoordeling

Positief advies

Datum:	21-10-2021
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL9813
Ander register	Leiden University Psychology Ethics Committee : 2021-03-23-A.W.M. Evers-V2-2998

Resultaten