An fMRI-study on the effects of NicVAX® and placebo on Central Nervous System activation and behaviour following a nicotine challenge.

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Main aim; to show that NicVAX attenuates nicotine induced CNS effects on brain activation and cognitive performance relative to placebo. The secondary aim; to evaluate how these changes in CNS stimulation alter subjective measures and the addictive...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON36778

Source
ToetsingOnline

Brief title
fMRI study NicVAX

Condition

- Other condition

Synonym
nicotine addiction, smoking

Health condition

De verslavende eigenschappen van nicotine en de mogelijke behandeling dmv vaccinatie worden onderzocht, rookgedrag levert een verhoogd risico op een scala van medische aandoeningen, preventie of vroege behandeling is daardoor gewenst.

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Maastricht
Source(s) of monetary or material Support: TOP Subsidie ZonMW

Intervention

Keyword: behaviour, fMRI, nicotine, vaccin

Outcome measures

Primary outcome

correlation between nicotine specific antibody and 1) the BOLD response during resting state, during the smoking-cue reactivity paradigm and during task performance; in regions of interest associated with the specific tasks; 2) the number of correct response and the reaction time;

Secondary outcome

Correlation between nicotine specific antibody and subjective signs of nicotine addiction, measured with several questionnaires

Study description

Background summary

Cigarette smoking is implicated in 20.000 (15%) of all deaths per year in the Netherlands. Most smokers are aware of the health consequences and want to quit, but have difficulty doing so. Only 3-5% of smokers who quit on their own are successful. Since the vast majority of those who attempt to quit will fail, the need for better approaches to smoking cessation is clear and urgent. Most effects of nicotine on the Central Nervous System (CNS) are directly mediated by nicotine molecules. A safe and effective means of blocking the effects of nicotine would be of considerable interest as a potential treatment for tobacco use and may be especially effective in the prevention of relapse. Treatment with NicVAX stimulates the production of nicotine specific

antibodies. These antibodies bind the small nicotine molecules, preventing them to cross the Blood Brain Barrier (BBB) and thus preventing CNS stimulation. A nicotine challenge given after vaccination will show no or diminished direct effects of nicotine on CNS stimulation. The blocking effects of the nicotine specific antibodies will be evaluated on several cognitive tasks and on reactivity to smoking-related cues.

Study objective

Main aim; to show that NicVAX attenuates nicotine induced CNS effects on brain activation and cognitive performance relative to placebo.
The secondary aim; to evaluate how these changes in CNS stimulation alter subjective measures and the addictive properties of nicotine.

To the best of our knowledge this will be the first fMRI study that investigates the effects of a nicotine challenge on brain activation after vaccination resulting in nicotine specific antibodies to attenuate these effects, while simultaneous evaluating the effects on cognitive performance, craving and mood.

Nicotine dependency and mood will be evaluated on every visit to the research centre; nicotine dependency will be evaluated again 6 months after vaccination to evaluate long term abstinence in correlation to brain activation in different testing conditions.
The results will help explain: (1) that NicVAX prevents the CNS effects of a nicotine challenge, (2) how direct effects of nicotine on the CNS might contribute to dependence, (3) whether smoking is sustained by transient enhanced performance or (4) to avoid cognitive deficits during abstinence; (5) how vaccination resulting in specific antibodies alters the CNS response to nicotine and the addictive properties of nicotine

Study design

within-subject cross-over (nicotine challenge) double-blind placebo controlled (vaccine) study

Intervention

The group will be randomised in two subgroups, one will recieve 5 injections with NicVAX, 4 weeks inbetween in the alternating deltoid muscle, the other group will recieve placebo vaccinations.
On the fMRI scanning sessions a nicotine challenge or placebo will be given in the form of Nicotine 2 mg chewing gum (randomised order).

Study burden and risks

Participants will complete a medical screening questionnaire (15-30 min) and will undergo a medical screening (45 min; 2 blood samples, a urine sample and an electrocardiogram). All participants will be vaccinated with NicVAX or Placebo 5 times on day 0, 28, 56, 84, 112 (4 weeks in between each injection) During the training session (Day 0; ±1,5 hour) the inclusion/exclusion criteria and baseline laboratory results will be reviewed to ensure that no changes to the participants health and eligibility status occurred since the Screening Visit. Participants will be randomized and receive either one dose NicVAX 400µ in 1 ml or a placebo intramuscular. The cognitive fMRI task will be trained in a dummy scanner, and questionnaires will be completed. Subsequent vaccinations (days 28, 56, 84, 112) should be given in the alternating deltoid muscle. Participants will be observed for 30 minutes to monitor possible adverse events. Adverse events, vital signs and concomitant medications will be recorded. During each test session (days 133, 140) participants will complete 5 questionnaires (30 minute total) and will perform several cognitive tasks inside the fMRI scanner (scan session in total 85 min). The last vaccination session (day 140) three blood samples will be taken for nicotine-specific antibody assessment and to monuitor any hematological/chemical changes (5 ml each).
In total the study will take 18 hours to complete. The participants will be paid 10 euro/hr as compensation. The risk of vaccination, fMRI scanning and of administration of nicotine 2mg gum (delivering a dose of approximately 1-1.5 mg nicotine to the bloodstream) is negligible for carefully screened participants. The nicotine specific-antibody vaccine has been clinically tested on several occasions; in these studies no major side-effects were reported. Local reactogenicity was mild to moderate and subsided spontaneously. The vaccine is associated with a decrease in smoked cigarettes per day and a higher success rate in quitting attempts; with lower relapse rates. The group receiving the vaccine could therefore in theory reduce smoking/exposure to tobacco smoke and have consequential health benefits.
There will be a financiaol compensation for time of 10.- per hour and a bonus of 35 euro for each scanning session. The maximum amount of payment is 380 euro per subject.

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

Male,18-45 years of age, smoking at least 10 cigarettes/day the last year, right handed in general good health

Exclusion criteria

Vaccination exclusion: allergic reactions, known immunodeficiencies, current or recent malignancy or chemotherapy
fMRI exclusion: claustrofobia, metalic implants etc, use of psychofarmaca
nicotine challenge: buccumucosal leasions

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial

Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	31-03-2011
Enrollment:	48
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NicVAX

Ethics review

Approved WMO Date:	24-03-2010
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	05-07-2010
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	02-08-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-09-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	22-03-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-06-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-07-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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
EudraCT	EUCTR2010-019381-90-NL
ClinicalTrials.gov	NCT01318668
CCMO	NL31915.000.10

Study results

Date completed:	31-10-2012
Actual enrolment:	48