Behavioural and physiological measures of the effects of norepinephrine on adapting to change

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The present project aims to determine the role of NE transmission in reactions to environmental change, both behavioral and psychophysiological, in healthy participants.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON38317

Source
ToetsingOnline

Brief title
Norepinephrine and adapting to change

Condition

- Other condition

Synonym
healthy volunteers, none

Health condition

geen

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit
Source(s) of monetary or material Support: NWO MAGW (Vidi aan M. Meeter)

Intervention

Keyword: behavior, brain, memory, Norepinephrine

Outcome measures

Primary outcome

Outcome parameters are: behavioral measures of the von Restorff effect, the novelty preference and the learning rate in a reinforcement-learning framework; and non-invasive electrophysiological measures in the form of event-related potentials. Our hypothesis is that Atomoxetine will lead to strengthened novelty responses, namely: higher amplitudes in the P3a and N2 components, a stronger von Restorff effect when evaluated with a bimodal (visual and auditory) task, higher novelty preference when tested with a visual paired comparison task, and higher learning rates.

Secondary outcome

Novelty-related personality traits using the TPQ questionnaire and the baseline memory span of the participants, and trait anxiety as estimated with the STAI personality test.

Polymorphisms of the following seven genes affecting the noradrenergic system: NET, DBH and COMT, and the alpha-1, alpha-2, beta-1, beta-2 adrenergic receptor genes.

Study description

Background summary

Several theorists have suggested that neuromodulatory systems are involved in the response of the brain to environmental change (Hasselmo & Barkai, 1995; Lisman & Grace, 2005). One of the neuromodulators of most interest in this regard is norepinephrine (NE). Microdialysis studies have shown increased levels of NE in the frontal cortex and the hypothalamus in response to novel environments (McQuade, Creton, & Stanford, 1999). Moreover, computational-modeling studies have suggested that NE plays an important role in optimizing inference and learning in dynamic environments (Yu & Dayan, 2005). However, no study has sought to manipulate norepinephrine levels to study its effects on responses to change.
Atomoxetine is a very selective norepinephrine reuptake inhibitor (SNRI), in contrast with other SNRIs that also affect the levels of dopamine and serotonin. It can therefore be used to investigate the role of norepinephrine in responding to changes in the environment.

It is not guaranteed that all participants will react in the same way to a Atomoxetine challenge. In particular, it is likely that the response will vary as a function of personality and genetic status. We will determine genotypes for genes related to the NE system and trait anxiety for each participant. Genetic variation has been shown to modulate responses to noradrenergic drugs (e.g., de Rover et al., in revision; Hughes, Watkins, Blumenthal, Kuhn, & Sherwood, 2004; Luksys, Gerstner, & Sandi, 2009; Mizuki, Suetsugi, Ushijima, & Yamada, 1996; Ressler & Nemeroff, 2000; White & Depue, 1999). Hence, including these measures may allow us to explain a potentially large part of the inter-individual variance in the effects of Atomoxetine on cognition.

Study objective

The present project aims to determine the role of NE transmission in reactions to environmental change, both behavioral and psychophysiological, in healthy participants.

Study design

Counter balanced within-subject (placebo controlled) design, using behavioral measures of response accuracy and electroencephalographic measures of brain activity (EEG) during execution of cognitive tasks. As covariates, personality traits and genotype will be measured.

Intervention

Single oral dose of atomoxetine (60 mg), and placebo, double-blind.

Study burden and risks

Participants will visit the EEG laboratory of the Faculty of Psychology (Van der Boechorststraat 1 building), on two separate occasions with 7 days in between to avoid carryover and reduce practice effects.
Pre-Testing: A personality questionnaire will be filled out before the first session by the internet, as a requirement for registration in the study. Before the intake of the drug, people will be tested with a memory span task, to determine their baseline level. Moreover, saliva will be collected to determine genotype with respect to several polymorphisms related to norepinephrine.
Day 1: First EEG recording. Half of the participants will receive Atomoxetine (60 mg), and the other half placebo, in a double blinded way. Participants will be asked to perform three tasks: an audiovisual task to evaluate the Von Restorff effect, a visual a visual paired comparison task, and a predictive inference task.
Day 2: Second EEG recording. Same as day one, but the groups receiving a placebo and Atomoxetine will be inverted.
None of the treatments and measurements causes any significant risk to the long-term health or well-being of the participants. Possible short-term side effects of the drug can include fatigue, headache, stomach ache, dizziness, drowsiness, vomiting, akathisia, and dry mouth.

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

personality questionnaire filled out
18-30 years old
informed consent
normal intelligence

Exclusion criteria

diagnosis of psychopathology
disease affecting brain function, such as epilepsy
smoking or self-reported drug abuse
use of medication, in particular antidepressants
pregnancy
history of heart disease
hypertension

Study design

Design

Study type:	Observational non invasive
Intervention model:	Crossover
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-10-2012
Enrollment:	32
Type:	Actual

Ethics review

Approved WMO

Date:	21-02-2012
Application type:	First submission
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
CCMO	NL33632.029.11