The role of the norepinephrine system in emotion, vigilance and error processing.

Published: 22-04-2009
Last updated: 18-07-2024

The primary objective of the current study is to investigate whether administered beta-blocker (propranolol) affects the following components of the EEG: the emotion-induced LPP, the vigilance-related P3, and the error-related Pe. To this end we...

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

Summary

ID

NL-OMON32686

Source
ToetsingOnline

Brief title
Norepinephrine system

Condition

- Other condition

Synonym
niet van toepassing

Health condition

focus op het gezonde brein

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Leiden
Source(s) of monetary or material Support: NWO-VIDI project dr SN Nieuwenhuis

Intervention

Keyword: EEG, emotion, propranolol

Outcome measures

Primary outcome

The main study parameter is the EEG measurement. The endpoint is the effect of propranolol on the EEG signal. We hypothesize that propranolol will decrease the amplitude of the different components of the EEG signal that we investigate.

Secondary outcome

The secondary study parameter is subsequent memory (% correctly recognized stimuli after the 2 week interval). The endpoint is the effect of propranolol on subsequent memory. We hypothesize that subsequent memory will be better for emotional than for neutral stimuli (higher % correctly recognized stimuli after the 2 week interval) and that this difference will decrease because of propranolol.

Study description

Background summary

In the field of cognitive neuroscience, interest in emotion is rapidly increasing. A critical distinction in this literature is the one between two affective dimensions: emotional intensity and emotional valence. Although a lot is known about the neural basis of valence, the neural basis of emotional intensity has so far been neglected. A well-known measure for emotional

intensity is the late positive potential (LPP): a specific component of the EEG signal. The LPP is highly sensitive to emotional intensity of stimuli and is larger for both pleasant and unpleasant than for neutral stimuli (Cuthbert et al., 2000; Keil et al., 2002; Lang et al., 1997; Schupp et al., 2000; Schupp et al., 2003). Because of its functional sensitivity the LPP has often been used as a tool to study the role of emotion in social behavior (Ito et al., 1998; Ito et al., 2004). Nonetheless, the neural basis of the LPP is largely unknown. The amplitude of the LPP was shown to significantly correlate with the brain activity in the visual cortex (Sabatinelli et al., 2007), whereas the human amygdala is well-known to be involved in the processing of emotional stimuli (Zald, 2003). A lesion study showed that increased visual cortex activation by emotional stimuli depends on an intact amygdala (Vuilleumier et al., 2004). Thus, it has been suggested that the recruitment of the amygdala in the processing of emotional stimuli activates the visual cortex, underlying the sensitivity of the LPP to the emotional intensity of stimuli (Dolcos & Cabeza, 2002; Vuilleumier, 2005).
In order to directly test this hypothesis, we intend to modulate emotional processing in the amygdala. This is usually done using beta-blockers, which are known to affect emotional memory by blocking the norepinephrine (NE) receptors (of the beta type) in the amygdala (Strange & Dolan, 2004). In the proposed research we will test directly whether modulation of emotional processing in the amygdala by the beta-blocker propranolol affects the LPP.
Another ongoing debate regarding the role of the NE system in cognition is about the so-called P3 component of the EEG signal (Nieuwenhuis et al., 2005). The P3 is typically observed when subjects perform a classic vigilance task: the oddball task, in which subjects have to detect the rare odd stimulus out of a series of standard stimuli. Animal research suggested that the P3 reflects the response of the NE system (Pineda et al., 1989; Pineda & Westerfield, 1993; Swick et al., 1994). An fMRI study in humans showed that oddball responses depend on activation of beta-type NE receptors (Strange & Dolan, 2007). However, it is still unknown whether the P3 in humans depends on activation of these receptors. In order to test this hypothesis we will investigate whether beta-blockers affect the P3 in humans during an oddball task.
The Pe component of the EEG signal is elicited when subjects make an error in typical choice reaction time tasks. It is considered to reflect affective processing of errors and is closely related to the P3 component (Leuthold & Sommer, 1999). However, it is still unknown whether the P3 and Pe are similarly modulated by the NE system. In order to test this hypothesis we will investigate whether beta-blockers affect the P3 in humans during the Eriksen Flanker task (Eriksen & Eriksen, 1974).
In behavioral cognitive neuroscience it is well known that emotional stimuli cause an interference effect (slowing down) in reaction time tasks like the Aproach-Avoidance task (Roelofs et al., 2005; Heuer et al., 2007; Roelofs et al., in press). However, it is still unknown whether the emotional intensity or the emotional valence of these stimuli causes the interference effect. To test this, we will measure the effect of propranolol on the interference effect as measured behaviorally in the emotional exogenous cueing task adapted from Fox

and colleagues (Fox et al., 2002) and in the approach-avoidance task (Heuer et al., 2006, adapted by Roelofs et al., 2008 for the NESDA study). Since propranolol decreases the effect of emotional intensity we expect that if the emotional intensity caused the interference effect, the interference effect should be decreased by propranolol. However, if the emotional valence caused the interference effect, propranolol should not affect the interference effect.

Study objective

The primary objective of the current study is to investigate whether administered beta-blocker (propranolol) affects the following components of the EEG: the emotion-induced LPP, the vigilance-related P3, and the error-related Pe. To this end we will measure EEG in healthy subjects twice, once on placebo and once on propranolol (80 mg, single dose).

Study design

While EEG is measured, participants will perform simple computertasks known to elicit the EEG components of interest (LPP, P3 and Pe) twice, once after taking 80 mg propranolol and once after taking a placebo (double-blind, cross-over design). The purpose of the study is to investigate the effect of propranolol on the EEG components of interest (see protocol for details).

Intervention

80 milligram propranolol in a capsule (once only). Propranolol is a non-selective beta-blocker mainly used in the treatment of hypertension, but also often used by musicians and other performers to prevent stage fright and performance anxiety. The usual maintenance dose ranges for oral propranolol therapy vary by indication: 120-320 mg daily in divided doses for hypertension and 10-40 mg 3-4 times daily for anxiety. We intend to administer 80 mg propranolol since this is a commonly used dose in cognitive research (eg. Maheu, Joober, Beaulieu, & Lupien, 2004; Maheu, Joober, & Lupien, 2005; van Stegeren et al., 2005) and we intend to use a single dose only. Metabolism occurs mainly by means of the kidneys. The biological half-life is 3-6 hours.

Study burden and risks

Cognitive computer tasks: There are no risks associated with the performance of cognitive computer tasks except the occasional possibility of some frustration with poor performance or fatigue. Testing will stop if a subject displays frustration or appears tired.

EEG: The EEG recording procedure used is standard for electrophysiological laboratories in hospitals and universities across the country. The only risk is some very minor skin irritation in a very small number of participants. This

requires no treatment and disappears within several minutes after the application of the electrode gel is complete. Participants* skin is never damaged. All the reusable materials that touch the subject*s skin are thoroughly washed and sterilized between uses, according to standard electrophysiological lab procedures. There is no risk of electrical shock.

Propranolol: Three earlier psychological studies with healthy subjects using 80 mg propranolol showed that this amount was well endured without side effects (Maheu, Joober, Beaulieu, & Lupien, 2004; Maheu, Joober, & Lupien, 2005; van Stegeren et al., 2005). Thus, the risks associated with a single dose of 80 mg propranolol is considered minimal. However, to reduce the remaining risks, strict prescreening procedures (chapter 4.3) and safety procedures (chapters 5.1 and 8.2) are in place.

Contacts

Public
Universiteit Leiden

Wassenaarseweg 52
2333AK Leiden
Nederland
Scientific
Universiteit Leiden

Wassenaarseweg 52
2333AK Leiden
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Adult subjects between the ages 18 and 30 with no history of neurological disorder/disease and normal blood pressure and heart rate will be included in this study. All participants will be right-handed native Dutch speakers.

Exclusion criteria

Low blood pressure, bradycardia, cardiac arrhythmia, severe pulmonary conditions, head trauma, learning disabilities, and history of neurological or psychiatric illness and/or use of (psychotropic) medication. Further, subjects with Dutch as a second language and left-handed individuals will be excluded.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-08-2009
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	22-04-2009
Application type:	First submission

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	18-07-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	24-07-2012
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL26019.058.08