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A study to evaluate the different levels of attention and VALence direction for erotic stimuli, in relation to genital and subjective sexual arousal in healthy female subjects and healthy female subjects with female sexual dysfunction

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23/08/2007

Registration date
23/08/2007

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19/09/2007

Recruitment status
No longer recruiting

Overall study status
Completed

Condition category
Mental and Behavioural Disorders

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.emotionalbrain.nl

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
EB069 (VAL)

Study information

Scientific Title

Acronym
VAL

Study objectives
In the present placebo controlled study we will investigate the influence of valence on attention when viewing visual erotic stimuli. Especially when under the treatment condition of testosterone with sildenafil. In addition, we will investigate the effects of testosterone in combination with sildenafil on vaginal and subjective sexual arousal induced by visual erotic stimuli in females with Female Sexual Dysfunction (FSD) and control subjects, for individual motivational and emotional differences (valence). In earlier study's we've found a distinction between groups that differ in colour naming of erotic words compared to neutral words. These two groups also differed in their benefit from testosterone combined with sildenafil.

We expect that for some women this treatment, testosterone with sildenafil will work adequately. For the other group, we expect that negative sexual experiences and personality differences and therefore the negative/defensive motivational neural circuit is responsible for the more diffuse reaction to the treatment of testosterone and sildenafil, in women with FSD.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval gained from the local ethics committee (Stichting Therapeutische Evaluatie Geneesmiddelen, Medische Etische Toetsingscommissie [STEGMETC]) on the 13th June 2007 (ref: R07-013).

Study design
Randomised, double-blind, placebo controlled, crossover trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)

Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Female sexual dysfunction

Interventions
Testosterone, administered as a solution sublingually (0.5 mg) and sildenafil, type 5 phosphodiesterase (PDE5) inhibitor, administered as an encapsulated tablet orally (50 mg):

Treatment A: 0.5 mg testosterone and sildenafil 50 mg
Treatment P: placebo testosterone and placebo sildenafil

The two treatments (A and P) will be randomised across the 120 subjects. Two different drug combinations will be given on separate days: (day 1) placebo, (day 2) sildenafil plus testosterone. Drug administration will be divided into two parts. Testosterone will be administered first. Two hours after testosterone administration, sildenafil (Viagra) will be administered. Testosterone will have a behavioural effect, increasing sexual desire and arousal, after four hours of intake. Sildenafil will have a physical effect, increasing blood flow to the genitals, after 1 hour of intake. It's duration is about six hours.

Two separate experimental days are separated by a three to ten day period.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Testosterone, sildenafil

Primary outcome measure
1. Evaluation of the women's judgment of valence (negative or positive) for erotic stimuli under placebo condition and the condition of 0.5 mg sublingual testosterone combined with sildenafil (50 mg) and the influence of positive and/or negative valence on attention for erotic cues, in healthy female subjects with and without Female Sexual Dysfunction.

Data for analysis:
1. Attention for erotic stimuli (strooptask: speedrate). A masked version of the Emotional Stroop Task comparing colour-naming latencies on neutral and erotic words will be used. The word is presented before and after the erotic film excerpts in the attention condition for about 24 ms and then masked by randomly cut, reassembled signs in the same colour (red, green, yellow or blue). The colour of the mask has to be assigned, and subjects are asked to verbally name the colours as quickly as possible. The stimuli are presented in the centre of the screen. An extra set of stimuli will be prepared for practice-trials. A trial consists of a fixation point, which will be shown for 750 ms, followed by the target stimulus (the coloured neutral or erotic word and

mask). Vocal responses will be recorded and will terminate the trials. The order of these 2 blocks will be randomly assigned. Attention will be measured on both the experimental days in the morning (pre-dose) and in the afternoon (post-dose).
2. Vaginal Pulse Amplitude (VPA. A vaginal photoplethysmograph will be used to measure Vaginal Pulse Amplitude (VPA) (the AC component of the signal), which is a reliable index for genital vasocongestion. Changes in the amplitude of the signal reflect changes in vaginal vasocongestion. The Vaginal Photoplethysmograph (VP) is a clean tampon shaped device, which contains an infrared Light-Emitting Diode (LED) as a light source and a photosensitive light detector (photodiode). It measures the blood volume in the tissue surrounding the plethysmograph. The light emitted by the LED is reflected by the blood vessels in the tissue. This light is measured by the photodiode. The output signal of the photodiode varies with changes in the amount of blood in the vessels. VPA will be measured on both the experimental days in the morning (pre-dose) and in the afternoon (post-dose)
3. Valence for erotic stimuli. Perceived emotional valence of erotic stimuli will be measured and compared to neutral, pleasant and unpleasant stimuli. Facial expressions reveal emotions with corresponding appetitive and defensive motivational circuits. The amygdala projects to the facial motor nucleus, which reflects the chosen motivational circuit; appetitive or defensive. Therefore, Electromyographic (EMG) activity will be measured over the corrugator, zygomatic major and orbicularis oculi muscles. Activation of the zygomatic muscle reveals a smile, but co-activation of the zygomatic and orbicularis mirrors a major smile. Activation of the corrugator muscle alone is correlated with viewing unpleasant events. More specifically, co-activation of the corrugator and orbicularis oculi reflects the emotion of repulsion and aversion. While viewing International Affective Picture System (IAPS) pictures (eight pictures for each domain; pleasant, neutral, unpleasant and erotic) and an additional category of sexually explicit pictures (depicting vaginal coitus), activation of the three muscles will be measured two seconds before picture onset and for six seconds during picture presentation. The activation of the orbicularis oculi muscle is also a component of the startle reflex. When viewing the pictures, half of all pictures will be accompanied by a startle stimulus. The acoustic startle stimulus consists of a 50-ms burst of white noise, presented at 95 dB. The startle stimuli will be presented through earplugs, between 3 and 5 seconds following picture onset. Prior to the first block, six startle sounds will be presented to allow habituation of the startle reflex. After the presentation of the pictures subjects are instructed to give a subjective rating of the emotional pictures by finger pointing at a touch screen. Each emotional picture will be followed by a picture of five figures with expressions ranging from happy (smiling) to unhappy (frowning). Subjects are instructed to rate on a 9-point scale how their feeling towards the preceding picture was reflected by one of the figures. The same was done for arousal, with excited, wide-eyed figures to sleepy, relaxed figures. Valence be measured on both the experimental days in the morning (pre-dose) and in the afternoon (post-dose).

Secondary outcome measures

1. To evaluate the correlation between subjective ratings of sexual functioning and physiological sexual responses
2. To evaluate the changes in differences in direction of valence when viewing visual erotic stimuli under the placebo condition and the condition with testosterone combined with sildenafil
3. To evaluate the individual differences in attention in relation to positive and/or negative valence induced by visual erotic stimuli
4. To evaluate the influence of personality traits on the differences in vaginal & subjective sexual arousal, EMG, valence direction and startle reflex
5. Subjective ratings of sexual functioning
6. Startle reflex
7. EMG activation

8. Personality traits
9. Negative sexual experiences will be assessed with a questionnaire and in the clinical interview, both during screening

Overall study start date
21/06/1978

Completion date
01/11/2007

Eligibility

Key inclusion criteria
40 Subjects must meet the following criteria:
1. Subjects must have a heterosexual orientation
2. Subjects must be between 21 and 65 years of age
3. Subjects with normal sexual functioning
4. Subjects must have signed the Informed Consent Form
5. Inclusion will be following the selection criteria including, but not limited to, a physical examination, gynaecological examination, medical history, vital signs, pregnancy test and Electrocardiogram (ECG)

80 Subjects must meet the following criteria:
1. Subjects must have a heterosexual orientation
2. Subjects must be between 21 and 65 years of age
3. Subjects must have experienced low sexual arousal and/or low sexual desire for at least six months prior to study entry according to Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition (DSM IV) criteria. The diagnosis will be made by an experienced psychologist /sexologist
4. Subjects must have signed the Informed Consent Form
5. Inclusion will be following the selection criteria including, but not limited to, a physical examination, gynaecological examination, medical history, vital signs, pregnancy test and ECG, and by the scoring on the strooptask during familiarization trial

Participant type(s)
Patient

Age group
Adult

Sex
Not Specified

Target number of participants
120

Key exclusion criteria
Subjects will not be eligible for inclusion if one of the following criteria applies:
1. Use of oral contraception containing anti-androgens (Like Diane 35 or Minerva)
2. Use of oral contraception containing 50 µg oestrogen or more

3. Pregnancy, or intention to become pregnant during this study (note: a serum or urine pregnancy test will be performed in all women prior to the administration of study medications)
4. A pelvic inflammatory disease or an untreated vaginal infection at screening
5. Lactating or subjects who have given birth in the previous six months
6. Previous prolapse and incontinence surgery affecting the vaginal wall
7. Women with other unexplained gynaecological complaints, such as abnormal uterine bleeding patterns;
8. History of endocrinological treatment or current endocrinological treatment (with the exception of the use oral contraceptives and of fertility-promoting treatment)
9. History of neurological treatment or current neurological treatment
10. History of serious psychiatric treatment or current psychiatric treatment
11. Any underlying cardiovascular condition including unstable angina pectoris, that would preclude sexual activity
12. History of myocardial infarction, stroke or life-threatening arrhythmia within the prior six months
13. Uncontrolled atrial fibrillation/flutter at screening (ventricular response rate greater than 100 bpm), or other significant abnormality observed on Electrocardiogram (ECG)
14. Systolic blood pressure greater than 140 mmHg and/or diastolic blood pressure greater than 90 mmHg. For subjects with age greater than 60 years and without diabetic mellitus, familiar hypercholesterolemia or cardiovascular disease: systolic blood pressure greater than 160 mmHg and/or diastolic blood pressure greater than 90 mmHg (according to the CBO-guideline hypertension [CBO.2000a])
15. Subjects who are taking strong CYP3A4-inhibitors: ritonavir (Human Immunodeficiency Virus [HIV] Protease inhibitor), ketoconazole and itraconazole
16. Subjects who are taking less strong CYP3A4-inhibitors: clarithromycin, erythromycine and saquinavir
17. Subjects who are taking CYP3A4-inducers: carbamazepine, phenytoin, phenobarbital, St Johns Wort, rifampicine
18. Severe chronic or acute liver disease, history of moderate (Child-Pugh B) or severe (Child-Pugh C) hepatic impairment
19. Use of medicinal herb as Ginkgo Biloba and nutrition containing grapefruit
20. Subjects who are taking nitrates or nitric oxide donors
21. A substance abuse disorder that in the opinion of the investigator is likely to affect the subject's ability to complete the study or precludes the subject's participation in the study; mild or moderately alcohol drinking behaviour is allowed, only 12 hours before the experimental days is alcohol drinking not allowed. Three weeks before the start of the experimental day is the taking of any recreational drug not allowed. Smoking is allowed
22. Use of any treatment for FSD within the seven days before visit one or during the study, including oral medications or constrictive devices
23. Subjects who are illiterate, unwilling or unable to understand and complete the questionnaires
24. Any other clinically significant abnormality or condition which in the opinion of investigator would interfere with the participant's ability to provide informed consent, comply with study instructions, possibly confound interpretation of study results, or endanger the participant if she took part in the trial
25. Moderate and severe hearing impairment
26. Subjects who are colour blinded
27. Subjects who are having botox® (or other equivalents of botox, like dysport) in the facial area within six months before the first experimental day

Date of first enrolment

21/06/1978

Date of final enrolment
01/11/2007

Locations

Countries of recruitment
Netherlands

Study participating centre
Emotional Brain BV
Almere
Netherlands
1311 RL

Sponsor information

Organisation
Emotional Brain B.V. (The Netherlands)

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Sponsor type
Industry

Website
http://www.emotionalbrain.nl/

ROR
https://ror.org/03vy5fy74

Funder(s)

Funder type
Industry

Funder Name

Emotional Brain B.V. (The Netherlands)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration