The Effect of Oral Contraceptive Onset on Emotion Regulation in Adolescence

Published: 16-09-2021
Last updated: 05-04-2024

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Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON50830

Source
ToetsingOnline

Brief title
A Bitter Pill

Condition

- Other condition
- Mood disorders and disturbances NEC

Synonym
anxiety and depression symptoms, mood problems

Health condition

sub-klinische depressie en angst scores en emotieregulatie metingen

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Adolescents, Contraceptive Pill, Emotion Regulation, Mood

Outcome measures

Primary outcome

The primary study parameters are the measurements regarding emotion regulation that are associated with fear and pill use in adults: the extent of fear acquisition and extinction by subjective measures and skin conductance (during the emotion regulation experiments).

Secondary outcome

The other study parameters include the Late Positive Potential (LPP) as a neural marker and electromyographie (EMG) as a physical marker for emotional reactivity that is modulated by emotion regulation (during the emotion regulation experiments) , and cortisol, self-evaluation and task performance changes after induced psychosocial stress (during the stress experiments), and mood questionnaires. These different study parameters are included to form a comprehensive view on the effects of the pill on neural, physiological and psychological processes underlying depression and anxiety in adolescents.

Study description

Background summary

Growing evidence into the effects of the oral contraceptive pill (*the pill*)

points to negative effects on mental health in pill users. Moreover, adolescent users appear to be most susceptible to pill-related mood and anxiety problems, these effects are possibly long-term due to the role of sex hormones in brain development. However, there is a surprising lack of research focusing on this high risk group and mechanisms behind the effect of the pill on depress ion and anxiety are still unknown.
Emotion regulation is an important mechanism in maintaining mental health, is associated with anxiety and depression and has an underlying neural network that is sensitivity to the hormones administered by the pill; estradiol and progesterone. Hence, this study will be the first to research whether starting pill use in adolescents leads to negative effects on emotion regulation on the level of neural, physiological and psychological processes. The findings will give insight into the effects of the pill on processes underlying mental health in new pill users. The current study will lead to progress of a scientific field which is still in its infancy. Additionally, the knowledge gained by this research is in line with the recently updated contraceptive directive from the Nederlands Huisartsen Genootschap (NHG) to inform contraceptive users about the psychological effects, and could contribute to improved communication between general practitioner and possible contraceptive user.

Study objective

The primary objective is to research whether the oral contraceptive pill in adolescents has a negative effect on emotion regulation in the form of fear acquisition and extinction. The secondary objective is to research whether a disruptive effect of pill use in adolescents is also evident in other forms and levels of emotion regulation, such as neural changes, emotion reactivity and regulation ability, physiological and psychological stress regulation, anxiety and depressive symptoms and mood fluctuations. Additionally, the influence of sex hormones, puberty phase, premenstrual symptoms, contraceptive-related side-effects and reason for pill use on the link between pill use and emotion regulation and mood will be researched.

Study design

The study comprises a between-subject design with within-subject measures in which the study is split into experiments into emotion regulation and experiments into stress effects. One group of adolescents that has requested a pill subscription from their GP on their own, will be asked to undergo a pre- and post-measurement around their first pill use for either the emotion regulation experiments or stress experiments. The tasks for the study are split into two separate experiments to reduce the burden on participants while simultaneously increasing feasibility of the study. Lab visits will take place just before the first pill intake and three months after pill onset. The control group consists of adolescents who haven't yet planned to start a

hormonal contraceptive.

Study burden and risks

The time costs consist of two lab visits of either 2:15 hours for the emotion regulation experiments and 1:45 hours for the stress experiments, and filling in a weekly short questionnaire (two minutes) during three months. Within the 4 test hours participants will fill in questionnaires, complete behavioral tasks and saliva and hair samples will be taken. During behavioral tasks an aversive scream and pictures with a negative emotional context will be presented during the emotion regulation experiments. During the stress experiments an unexpected task will be used to elicit short-term stress and anxiety. Questionnaires will be administered about mood, demographics, drugs and alcohol use, youth trauma, partner status, puberty phase, premenstrual symptoms , contraceptive-related side-effects and reason for pill use. In addition, saliva and hair samples will be collected for hormone measurements. The risks of the study are negligible. The time costs of the study is limited (and as a result increases feasibility) by splitting the study into the separate emotionregulation and stress experiments. The biggest burden of the study concerns the aversive stimuli (noise, negative images) and the induced stress. These aversive stimuli are necessary to measure the different facets of emotion regulation that can be influenced by hormones: behavioral, experiential, physiological and neural. The strain on participants will be minimalized by limiting the emotional discomfort to the experimental setting and limiting the frequency and time of the stimuli presentation. The participants will be explicitly asked whether they want to continue participation after practice rounds. There is no risk of long-term negative effects related to the study, since the stimuli have been used in previous validated and common experiments that are also administered to adolescents. The scientific and societal relevance of this study outweighs the minimal burden. This will be the first study that researches a causal effect of the pill on different forms and levels of emotion regulation to elucidate the mechanisms by which the pill increases vulnerability to anxiety and depression in girls. The elegance of the proposed study design lies in the absence of an active intervention, in which participants will be followed during their self-chosen start of the contraceptive pill. The research is group restricted since the brain of adolescents is very sensitive to sex hormones and it is likely that the effects of the pill manifest differently than in adult users. Accordingly, previous research suggests that adolescents have an increased and possible long term sensitivity to the negative effects of the pill. In addition, there is a lack of within-sub ject research that focuses on wamen younger than 18 years old. There is a benefit for the group since the outcomes of the study could result in potential pill users and prescribers making a better informed decision around starting pill use during adolescence. The results could also indicate that a follow-up for psychological side effects after starting the pill is especially relevant for adolescents and possibly requires offering alternative contraceptive options. Besides the focus of this study on clinically relevant changes in mood, researching the effects on

emotion regulation makes it possible to identify a more subtle risk on anxiety and mood disorders at a later age for this group of contraceptive users.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)

Inclusion criteria

• Healthy (no somatic or psychiatric diagnoses)
• 14-18 years
• Body Mass Index (BMI) between 14-30
• Regular menstrual cycle (25-32 days)
• Pillgroup: girls who will start the use of the oral contraceptive pill for the first time or after a break of minimum 6 months (assuming the use of the standard prescription of ethinylestradiol/levonorgestrel 0,03/0,15 mg; a pill

with androgenic function, however other androgenic pills will also be included)
• Control group: girls who have never taken hormonal contraceptives or not taken hormonal contraceptives for at least the past 6 months

Exclusion criteria

• Starting an oral contraceptive pill with anti-androgenic function after the first lab visit
• Use of hormones 6 months before study onset
• Use of psychotropic medication/drugs three months before study onset
• Pregnant or breastfeeding
• Hormone disorders
• Endometriosis
• Polycystic ovarian syndrome (PCOS)
• Current or previous diagnosed psychiatric or neurological disorders (self-report)
• Participants will be asked to prevent intake of marijuana (>48h), alcohol (>24h) and caffeine (>2h) before onset of the experiment.

Study design

Design

Study phase:	4
Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2021
Enrollment:	126
Type:	Anticipated

Ethics review

Approved WMO Date:	16-09-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	24-01-2022
Application type:	Amendment
Review commission:	METC NedMec

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	NL77555.041.21