Do adverse childhood experiences influence sensitivity to side-effects and reward behavior on hormonal contraceptives?

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Background

• Hormonal contraceptives (HC) are frequently discontinued due to emotional and sexual side-effects, increasing risk of unplanned pregnancy (1).

• Compared with endogenous estradiol and progesterone, hormone analogs used in HC may decrease aspects of reward processing such as motivation for reward or the ability to feel pleasure (2,3).

• Adverse childhood experiences (ACE) prior to puberty are associated with both deficits in reward processing (5) and negative neuropsychiatric effects due to changes in ovarian steroids (4).

Objectives

• Evaluate the influence of ACE on decreased reward processing on HC via a large-scale cross-sectional study using an online reward task.

• Using cross-sectional data, design a placebo-controlled fMRI study to investigate the neural effects of HC on reward processing in vulnerable women.

Methods

• N = 1029 women (N=541 on HC, N=488 not on HC) in generally good health, between the ages of 18-40.

• Participants completed an online reward task based on Jepma et al (8) and Wilroth et al (9) designed to evaluate reward expectancy and reward responsiveness for non-erotic pleasant images, erotic images and neutral images.

Fig 1. Reward Task

• Participants completed surveys on demographic information, health history, depression, anxiety, stress, and relationship experiences.
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Results

Table 1: Selected Demographics

<table>
<thead>
<tr>
<th>Demographics variable</th>
<th>Female study completers (N = 1029)</th>
<th>Females non-HC (N = 488)</th>
<th>Females HC (N = 541)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>28.7 (5.2)</td>
<td>29.0 (5.6)</td>
<td>28.5 (4.8)</td>
<td>0.125</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td>0.012</td>
</tr>
<tr>
<td>Asian</td>
<td>78 (7.6%)</td>
<td>46 (9.4%)</td>
<td>32 (5.9%)</td>
<td></td>
</tr>
<tr>
<td>Black or African American</td>
<td>40 (3.9%)</td>
<td>26 (5.3%)</td>
<td>14 (2.6%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>844 (82.0%)</td>
<td>383 (78.5%)</td>
<td>461 (85.2%)</td>
<td></td>
</tr>
<tr>
<td>Other/multiracial</td>
<td>67 (6.5%)</td>
<td>33 (6.8%)</td>
<td>34 (6.3%)</td>
<td></td>
</tr>
<tr>
<td>Sexual orientation</td>
<td></td>
<td></td>
<td></td>
<td>0.085</td>
</tr>
<tr>
<td>Heterosexual</td>
<td>802 (77.9%)</td>
<td>373 (76.4%)</td>
<td>429 (79.3%)</td>
<td></td>
</tr>
<tr>
<td>Bisexual</td>
<td>156 (15.2%)</td>
<td>75 (15.4%)</td>
<td>81 (15.0%)</td>
<td></td>
</tr>
<tr>
<td>Homosexual/gay/lesbian</td>
<td>35 (3.4%)</td>
<td>24 (4.9%)</td>
<td>11 (2.0%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>36 (3.5%)</td>
<td>16 (3.3%)</td>
<td>20 (3.7%)</td>
<td></td>
</tr>
<tr>
<td>Relationship status</td>
<td></td>
<td></td>
<td></td>
<td>0.003</td>
</tr>
<tr>
<td>In a relationship</td>
<td>684 (66.5%)</td>
<td>300 (61.5%)</td>
<td>384 (71.0%)</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>345 (33.5%)</td>
<td>188 (38.5%)</td>
<td>157 (29.0%)</td>
<td></td>
</tr>
<tr>
<td>Highest education level</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High school diploma or less</td>
<td>172 (16.7%)</td>
<td>107 (21.9%)</td>
<td>65 (12.0%)</td>
<td></td>
</tr>
<tr>
<td>College degree</td>
<td>499 (48.5%)</td>
<td>224 (45.9%)</td>
<td>275 (50.8%)</td>
<td></td>
</tr>
<tr>
<td>Master’s/professional degree</td>
<td>358 (34.8%)</td>
<td>157 (32.2%)</td>
<td>201 (37.2%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Types of Hormonal Birth Control in HC group.

<table>
<thead>
<tr>
<th>Hormonal birth control type</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hormonal IUD</td>
<td>227 (42.4%)</td>
</tr>
<tr>
<td>Implant</td>
<td>35 (6.5%)</td>
</tr>
<tr>
<td>Oral contraceptive pills</td>
<td>246 (45.9%)</td>
</tr>
<tr>
<td>Injections</td>
<td>6 (1.1%)</td>
</tr>
<tr>
<td>Vaginal ring</td>
<td>22 (4.1%)</td>
</tr>
</tbody>
</table>

Adverse Childhood Experiences (ACE) and Current HC Use

![Graph showing the comparison between low ACE and high ACE on hormonal contraceptives](chart.png)

Fig 2. Significantly greater proportion of women with low ACE on HC compared to women with high ACE (p=0.043).
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Results

Fig 3. Proportion of women reporting mood and sexual side-effects from HC was significantly greater among those with high ACE vs low prepubertal ACE (p=0.033).

Fig 4 and 5. Significant interactions between prepubertal ACE and HC use for average expected (p=0.029) and experienced (p=0.025) valence ratings for erotic images. #Among those not on HC, women with high ACE had increased expected (p=0.0025) valence ratings vs low ACE. *Among low ACE women, those on HC had higher experienced valence ratings vs. no HC (p=0.022).
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Summary

- ACE may increase risk of HC-induced side-effects related to mood and sexual function (Figs 2, 3)
  - ACE known to increase vulnerability to negative neuropsychiatric effects of hormonal changes (4).
- In women not on HC, high prepubertal ACE might increase reward anticipation to erotic stimuli but not other pleasant stimuli (Figs 4, 5)
  - Overall, prepubertal ACE associated with decreased reward anticipation and responsiveness (5).
  - However, some evidence that ACE sensitizes individuals to sexual stimuli (6).
- In women with low prepubertal ACE, HC might increase reward sensitivity to erotic stimuli (Figs 4, 5)
  - HC known to improve sexual function in some women (7).
  - Pharmacological effect of HC vs other factors? Survivor effect?
- Unlike women with low prepubertal ACE, women with high prepubertal ACE taking HC did not have indications of higher reward sensitivity to erotic stimuli compared to those not taking HC
  - While other factors likely, survivor effect may have masked decreased reward sensitivity among high ACE women on HC.

Future Directions: Planned Placebo-Controlled Study of HC and reward processing

Main Outcome Measures:
1. Expected and Experienced Valence Ratings of Images
2. Neural activity during reward expectation and receipt in reward sensitive brain regions (nucleus accumbens and medial prefrontal cortex)
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References


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