



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.

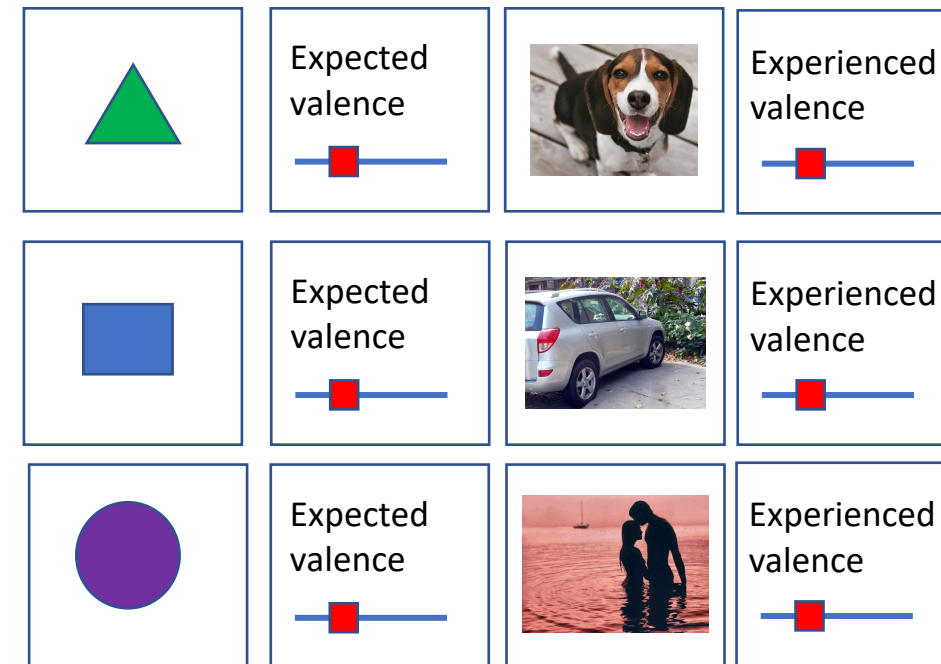


Fig 1. Reward Task

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



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Results

Table 1: Selected Demographics

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

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

Hormonal birth control type	N (%)
Hormonal IUD	227 (42.4%)
Implant	35 (6.5%)
Oral contraceptive pills	246 (45.9%)
Injections	6 (1.1%)
Vaginal ring	22 (4.1%)

Adverse Childhood Experiences (ACE) and Current HC Use

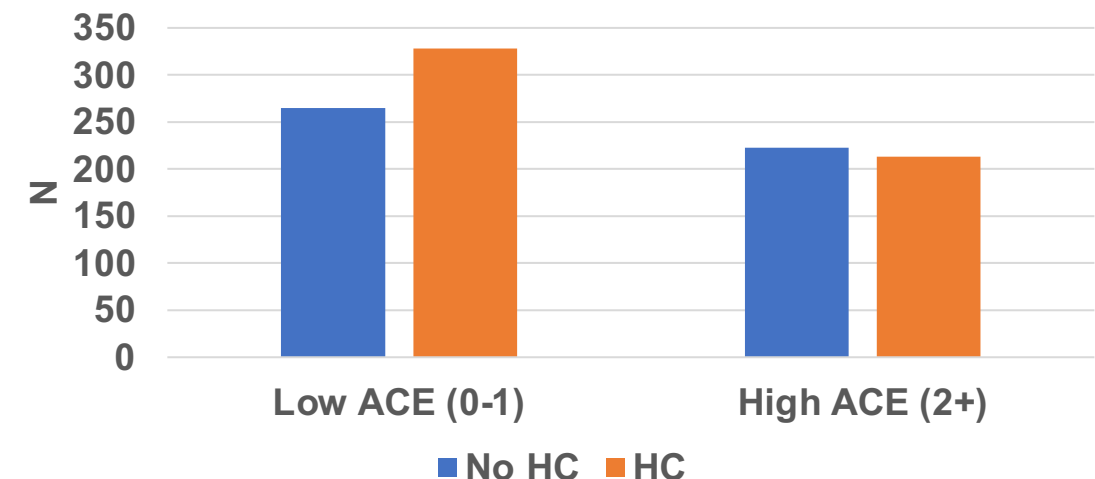


Fig 2. Significantly greater proportion of women with low ACE on HC compared to women with high ACE (p=0.043).



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Fig 3: Current or Previous Mood or Sexual Side-effects from HC and Prepubertal ACE

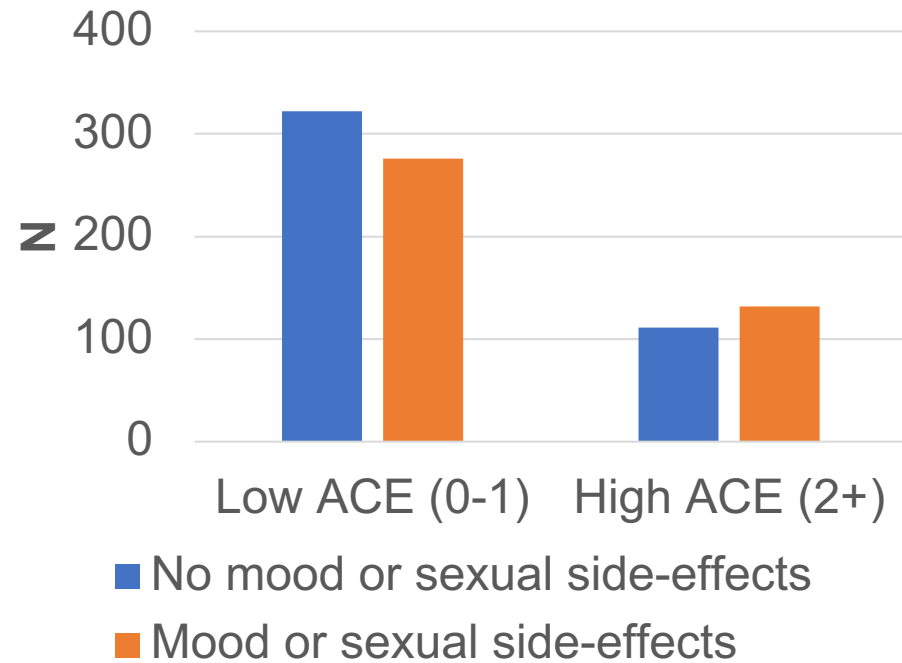


Fig 3. Proportion of women reporting mood and sexual side-effects from HC was significantly greater among those with high ACE vs low prepubertal ACE (p=0.033).

Fig 4. Prepubertal ACE, HC Use and Expected Erotic Image Valence Rating

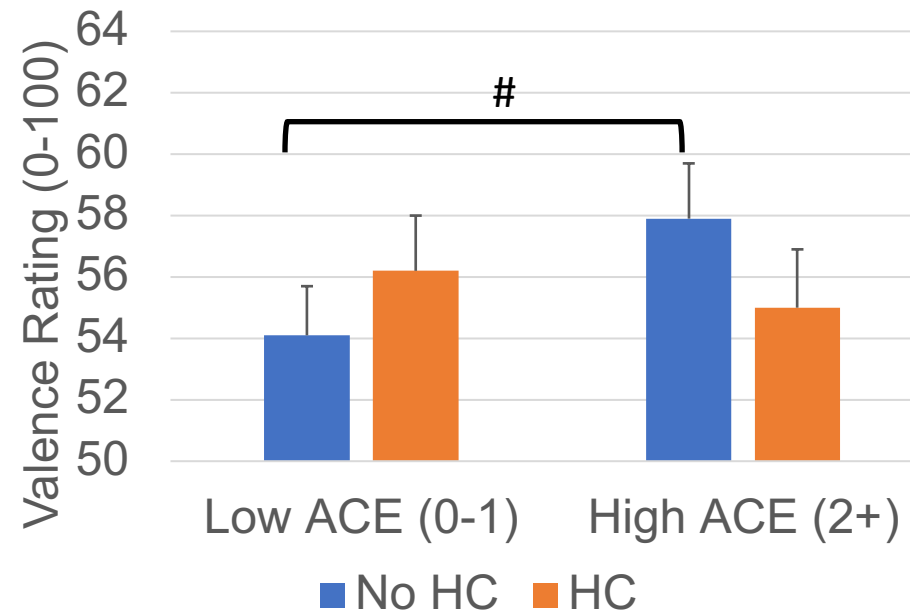
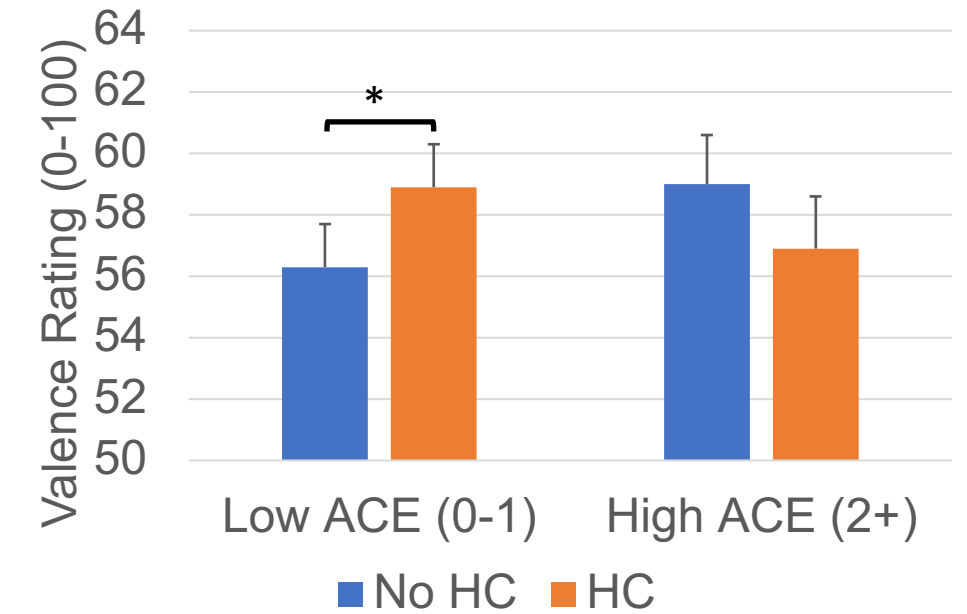


Fig 4 and 5. Significant interactions between prepubertal ACE and HC use for average expected (p=0.029) and experienced (p=0.025) valence ratings for erotic images. #Among those not on HC, women with high ACE had increased expected (p=0.0025) valence ratings vs low ACE. *Among low ACE women, those on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

Fig 5: Prepubertal ACE, HC Use and Experienced Erotic Image Valence Rating





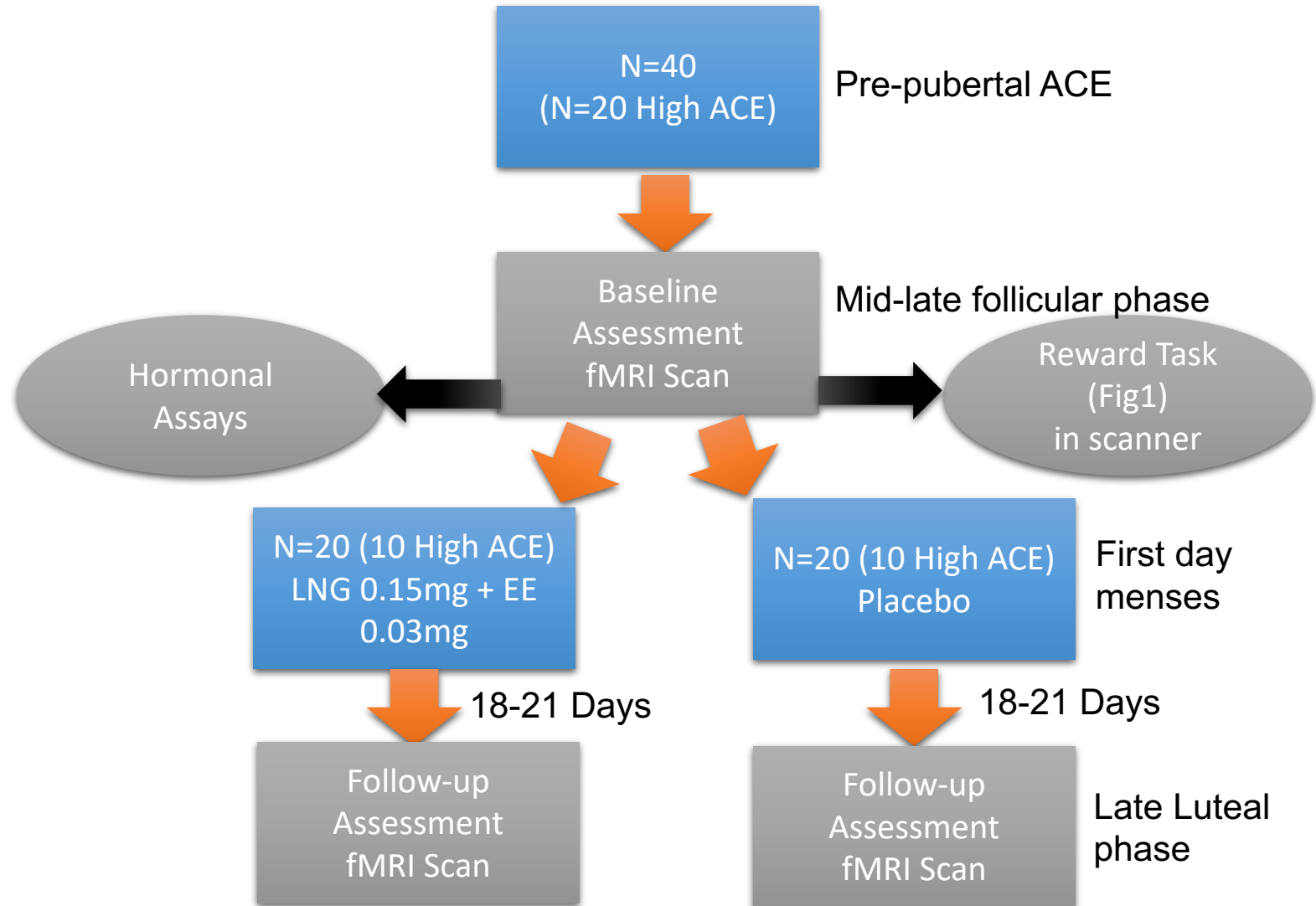
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Summary

- 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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