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Original Research

Reduction in genital sexual arousal varies by type of oral contraceptive pill

Ariel B. Handy, PhD[1,*], Leah N. McMahon, BSA[2], Irwin Goldstein, MD[3], Cindy M. Meston, PhD[2]

[1]Department of Psychology, McLean Hospital, Belmont, MA 02478, United States
[2]Department of Psychology, University of Texas at Austin, Austin, TX 78712, United States
[3]Department of Sexual Medicine, Alvarado Hospital, San Diego, CA 92120, United States

*Corresponding author: Department of Psychology, McLean Hospital, Belmont, MA 02478, United States. Email: arielbhandy@gmail.com

Abstract

Background: Although oral contraceptive pills (OCPs) have been associated with decrements in self-reported genital arousal and vaginal lubrication,[1,2] little is known about how these outcomes vary across types of OCPs.
Aim: The present study examined differences in physiological lubrication and vaginal blood flow, as well as rates of self-reported vulvovaginal atrophy and female sexual arousal disorder, among women using OCPs with varying androgenic properties.
Methods: Participants in this study were 130 women: 59 naturally cycling control women, 50 women taking androgenic OCPs, and 21 women taking antiandrogenic OCPs. Participants watched sexual films while their sexual arousal responses were measured, completed questionnaires, and participated in a clinical interview.
Outcomes: Vaginal blood flow, vaginal lubrication, self-reported vulvovaginal atrophy, and female sexual arousal disorder were assessed.
Results: Results indicated deficits in vaginal pulse amplitude and lubrication for women taking either form of OCP, with marked inhibitory effects found in women taking antiandrogenic OCPs. Rates of self-reported vulvovaginal atrophy and female sexual arousal disorder were also significantly greater in the antiandrogenic group compared with the control group.
Clinical Implications: It is recommended that prescribing clinicians consult patients on such physiological effects of OCPs.
Strengths and Limitations: To our knowledge, this was the first study to compare multiple measures of physiological sexual arousal across groups of women taking OCPs with varying hormonal profiles. Because all OCPs included in this study contained low doses of ethinylestradiol, we were able to identify the specific effects of the androgenic properties on women's sexual arousal responses. However, the self-administered lubrication test strip was subject to user error. Additionally, the generalizability of findings is limited by the largely heterosexual and college-aged sample.
Conclusion: Compared with naturally cycling women, women taking OCPs that contain antiandrogenic progestins experienced decreased vaginal blood flow and lubrication as well as higher rates of self-reported vaginal bleeding and female sexual arousal disorder.

Keywords: sexual arousal; sexual health; oral contraceptive pills; hormonal contraceptives.

Introduction

Genital sexual arousal, which consists of genital vasocongestion and lubrication, is critical to healthy sexual function in women and is closely linked with hormone function. Estrogens and androgens play important roles in maintaining the physiological integrity of many tissues, including vulvar and vaginal tissue.[1,2] They do so by regulating distinct cellular processes within the tissue of the vulva and vagina, such as the growth and function of neurons, blood vessels, smooth muscle, and cells within the endothelium and epithelium.[3,4] This keeps capillary beds lush and tissue healthy. The importance of estrogen for vaginal tissue is perhaps most clearly evidenced in women transitioning into menopause. Estrogen deprivation often leads to vulvar and vaginal atrophy; however, symptoms may remit with locally administered estrogen or dehydroepiandrosterone.[5] Estrogens are critical for maintaining healthy vaginal physiology. Androgens, on the other hand, are present throughout the clitoris, vulva, and vaginal mucosa.[6] Androgens also have distinct vasodilatory effects,[7] which enhance blood flow and likely subsequent lubrication. The precise role of androgens on vaginal blood flow and tissue structure is unknown,[8] but researchers have theorized that androgens and estrogens may interact to facilitate sexual arousal. As such, disturbances to optimal levels of androgens and estrogens may hinder physiological sexual arousal responses.

Oral contraceptive pills (OCPs) are used by over a quarter of reproductive-age women in the United States.[9,10] Some of the side effects of OCPs are well known (eg, menstrual regulation)[11]; however, the influence of these drugs on sexual function is unclear. Whereas some studies report improvements in sexual function,[12] several recent reviews have suggested that OCPs may hinder physiological processes such as lubrication.[6,13–15] Indeed, one Internet-based cross-sectional study found that women taking OCPs reported greater levels of vaginal dryness and sexual pain as well as decreased lubrication, arousal, pleasure, and orgasm frequency compared with women using nonhormonal forms of contraception.[16] Smith et al[17] suggested that these findings may be related to decreases in bioavailable androgens and direct structural effects of OCPs on the vagina; however, they did not conduct separate analyses for the type of hormonal contraceptive used. Indeed, OCPs tend to reduce the number of bioavailable androgens through the upregulation of sex hormone binding globulin,[18] but the potency of this effect may vary across different types of OCPs.

In the United States, almost all combined OCPs contain ethinylestradiol, a synthetic estrogen, and a progestin. Though

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OCPs containing bioidentical or natural forms of estrogen are available (eg, estradiol valerate, 17 β-estradiol), they are less frequently prescribed in the United States. The specific progestins included in OCPs are derived from 1 of 4 main families: 19-nortestosterone (estranes and gonanes), 17α-hydroxyprogesterone (pregnanes), 19-norprogesterone (norpregnanes), and spironolactone.[19] Each family of progestin has different levels of androgenicity. Progestin androgenicity is defined as the extent to which the progestin increases hepatic production if sex hormone binding globulin, which binds to and therefore reduces the amount of bioavailable testosterone.[19] Derivatives of 19-nortestosterone tend to lack androgenic effects (ie, has little to no impact on testosterone), derivatives of 19-norprogesterone have varying degrees of androgenic activity (ie, minimally reduces testosterone), and 17α-hydroxyprogesterone derivatives and drospirenone, the sole derivative of spironolactone, may exert antiandrogenic (ie, antagonistic; maximally reduces testosterone) activity.[19] Given the importance of estrogens and androgens and potential inhibitory role of certain progestins in genital blood flow and subsequent lubrication, it is possible that combined OCPs containing antiandrogenic progestins (eg, 17α-hydroxyprogesterone derivatives, drospirenone) may hinder female sexual arousal. Indeed, one prospective study found that women experienced decreased thickness of the labia minora, reduced diameter of the vulvar vestibule, and reduced clitoral blood flow after 3 months of receiving an OCP containing the progestin drospirenone, which has strong antiandrogenic effects.[20]

The well-documented relationships between sex steroid hormones and sexual function in women[3,4,21] coupled with the mainstream use of OCPs makes clarifying the sexual side effects of these drugs imperative. Several recent and well-conducted reviews on this topic suggest that hormonal contraceptives negatively impact sexual desire and vaginal lubrication.[13–15] However, as suggested by de Castro et al and others,[13–15] the nuances of the impacts of estrogens and progestins on female sexual function need further investigation. To further this line of research, the present study examined the effects of OCPs with specific hormonal concentrations on women's physiological sexual arousal responses (ie, vaginal pulse amplitude and lubrication), self-reported vulvovaginal atrophy, and the presence of female sexual arousal disorder. We hypothesized that women taking antiandrogenic OCPs would demonstrate the lowest vaginal pulse amplitude and lubrication, the highest rates of self-reported vulvovaginal atrophy, and the highest incidence of female sexual arousal disorder. We hypothesized that these effects would be present, though less pronounced, in women taking androgenic OCPs. In contrast, we hypothesized women in the control group would display the highest vaginal pulse amplitude and lubrication, the lowest rates of self-reported vulvovaginal atrophy, and the lowest incidence of female sexual arousal disorder.

Methods

Participants

Participants were recruited through online advertisements and flyers posted throughout the local community, as well as through the Human Subjects Pool in Psychology at the University of Texas at Austin. All advertisements invited women to call the laboratory for a phone eligibility screening. Inclusion criteria included being 18 of 35 years of age, fluent in English, and currently sexually active, and either currently taking an androgenic or antiandrogenic OCP or having no history of taking any hormonal contraceptives.

Androgenicity was determined using guidelines published by an expert panel.[22] Antiandrogenic OCPs were defined as OCPs containing low-dose ($\leq$25 μg) ethinylestradiol plus a progestin that is a 17α-hydroxyprogesterone derivative (eg, cyproterone acetate) or drospirenone. Androgenic OCPs were defined as OCPs containing low-dose ($\leq$25 μg) ethinylestradiol plus a progestin that is a derivative of 19-nortestosterone (eg, levonorgestrel). To allow the body to adjust to changes in hormone concentrations, it was further required that women in both contraceptive groups had been taking their OCP for at least 3 months to qualify for participation; see Battaglia et al[20] for documentation of vaginal changes after 3 months of OCP use.

Exclusion criteria included being pregnant or currently breastfeeding; currently taking beta-blockers, antidepressants, anxiolytics, antipsychotics, or any medical treatments to enhance sexual response; currently receiving exogenous hormones or hormone precursors (eg, dehydroepiandrosterone); currently experiencing stress or urinary incontinence; having a history of a medical condition known to affect hormone function; having a history of major pelvic surgery that caused nerve damage; having a history of childhood sexual abuse; or having a history of Sjögren's or related syndromes.

Eligible women were invited to schedule a clinical interview and experimental session at the University of Texas at Austin. As OCPs mimic the body's natural postovulatory hormonal concentrations,[23] all naturally cycling women were scheduled to participate in the laboratory session during the luteal phase (ie, between days 14 and 28) of their menstrual cycle. This also served as a method of gaining conservative estimates of possible between-group differences, as greater levels of sexual function are typically observed during the follicular phase of women's menstrual cycles.[24–28] Women taking OCPs were also scheduled during days 14 to 28 for consistency.

Participant characteristics

A power analysis indicated that 123 participants would be required to identify a small effect ($f = 0.2$) in a 2-tailed design with 90% power. In total, 130 women participated in this study, with 59 women in the control group, 50 women in the androgenic group, and 21 women in the antiandrogenic group. Nearly all women (n = 45, 90%) in the androgenic group reported currently taking OCPs containing 20 μg ethinylestradiol, and 34 (68.00%) women in this group were taking OCPs with 1 mg norethindrone acetate. Most women (n = 20, 95.23%) in the antiandrogenic group similarly reported using an OCP with 20 μg ethinylestradiol, and the majority of these women (n = 13, 61.90%) were taking an OCP containing 3 mg drospirenone.

On average, women in this study were 20.12 $\pm$ 2.53 years of age. Three-quarters (74.61%) of the participants identified as heterosexual, 33.07% of the sample identified as Caucasian, and roughly half (55.38%) reported being in a committed relationship. The average relationship length was 19.26 $\pm$ 19.19 months (ie, roughly 1.5 years). Three-quarters (76.92%) of the participants reported having completed some college, and 43.84% reported a household income of <$50 000. Refer to Table 1 for demographic characteristics for each group and Table 2 for a complete list of the OCPs used by study participants.

Table 1. Demographic characteristics for participants in each study group.

	Control (n = 59)		Androgenic (n = 50)		Antiandrogenic (n = 21)		
Continuous variables	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	***F***
Age, y	19.98	3.08	20.20	1.88	20.33	2.26	0.182
Relationship length, mo	22.05	24.00	18.39	16.48	14.94	9.84	0.827
Duration of OCP use, mo	—	—	23.42	18.90	21.10	19.87	—
Discrete variables	**n**	**%**	**n**	**%**	**n**	**%**	χ^2
Orientation							11.336
Heterosexual/straight	42	71.18	40	80.00	15	71.42	
Bisexual	11	18.64	6	12.00	5	23.80	
Homosexual/gay/lesbian	3	5.08	—	—	—	—	
Other	3	5.08	4	8.00	1	4.76	
Relationship status							12.825
Single	28	47.45	23	46.00	4	19.04	
Committed relationship	30	50.84	25	50.00	17	80.95	
Married	1	1.69	—	—	—	—	
Other	—	—	2	4.00	—	—	
Race							18.499[a]
African American/Black	8	13.55	1	2.00	3	14.28	
Asian	16	27.11	13	26.00	3	14.28	
Caucasian/White	11	18.64	25	50.00	7	33.33	
Hispanic	20	33.89	11	22.00	7	33.33	
Other	4	6.77	—	—	1	4.76	
Education							11.338
High school diploma/GED	9	15.25	3	6.00	—	—	
Some college	43	72.88	41	82.00	16	76.19	
College degree	7	11.86	4	8.00	5	23.80	
Advanced degree	—	—	2	4.00	—	—	
Household income							5.663
<$50 000	28	47.45	20	40.00	9	42.85	
$50 000-$100 000	20	33.89	12	24.00	4	19.04	
>$100 000	11	18.64	18	36.00	8	3.80	

Abbreviations: GED, general education diploma; MA, master's degree; OCP, oral contraceptive pill. [a] $P = .017$; insignificant after Bonferroni correction

Measures

Diagnostic interview

All participants underwent a brief, clinician-administered diagnostic interview to gather information regarding the presence or absence of sexual arousal concerns, based on International Classification of Diseases–Eleventh Revision and DSM-IV-TR female sexual arousal disorder criteria.[29,30] In the interview, the clinician assessed for past and current ability to become sexually aroused, the nature of any concerns (if present), duration of symptoms, and associated distress.

Vaginal blood flow

A vaginal photoplethysmograph[31] was used to assess women's genital blood flow in response to the film presentations. The vaginal pulse amplitude (VPA) signal was sampled at a rate of 200 samples per second throughout the entire 240 seconds of neutral film presentation and 360 seconds of erotic film presentation. Each wave was recorded in millivolts, bandpass filtered (0.5-30 Hz), and recorded on a computer in the next room using the software program AcqKnowledge III (version 3.8.1) and a Model MP150 data acquisition unit (BioPac Systems, Inc) for analog and digital conversion.

Lubrication

Lubrication was measured with the Schirmer Tear Test strips, a test that previous research has shown to be sensitive enough to detect changes in vaginal lubrication induced by sexual films.[32] The test strips are ruled in millimeter increments and are 40 mm in length. In this assessment, a paper test strip is applied directly to the vaginal membrane for 60 seconds, both before and after exposure to stimuli. The amount of moisture absorbed into the test strip is immediately measured. In an attempt to standardize the depth of insertion of these test strips, they were adhered to wooden applicators beginning at 5 mm, thus allowing for only the first 5 mm to be inserted into the vaginal opening consistently across participants.

Self-reported vulvovaginal atrophy assessment

Symptoms of self-reported vulvar and vaginal atrophy were assessed with a 5-item measure that is commonly implemented in Food and Drug Administration trials assessing vaginal health.[33] In this measure, participants rate the severity of the following symptoms on a 4-point Likert-type scale ranging from 0 (mild) to 3 (severe): vaginal dryness, vaginal and/or vulvar irritation/itching, dysuria, and vaginal pain associated with sexual activity. Participants also dichotomously rate the presence or absence of vaginal bleeding associated with sexual activity.

Procedure

Upon arrival to the laboratory, participants received an explanation of all study procedures and instruments, and they signed the Informed Consent Document. Women then participated in a brief diagnostic interview assessing the presence or absence of female sexual arousal disorder. Following this interview, women received a labeled diagram of the vulvar region and detailed instructions on how to perform the lubrication measurement, insert the vaginal photoplethysmograph, and attach electrocardiogram electrodes. As it is presently

Table 2. List of OCPs and compositions for each of the 2 OCP groups.

Brand name	Estrogen dose (mg)	Progestin	Progestin dose (mg)	Androgenicity	n
Low-dose ethinylestradiol + androgenic progestin					
Blisovi	0.02	Norethindrone acetate	1.00	1.60	13
Gildess	0.02	Norethindrone acetate	1.00	1.60	2
Junel	0.02	Norethindrone acetate	1.00	1.60	11
Kaitlib Fe	0.025	Norethindrone	0.80	0.80	1
Larin	0.02	Norethindrone acetate	1.00	1.60	1
Lo lestrin Fe	0.01	Norethindrone	1.00	1.00	4
Loestrin	0.02	Norethindrone acetate	1.00	1.60	2
Lupin	0.02	Levonorgestrel	0.10	0.83	1
Lutera	0.02	Levonorgestrel	0.10	0.83	2
Mibelas	0.02	Norethindrone acetate	1.00	1.60	1
Microgestin	0.02	Norethindrone acetate	1.00	1.60	4
Mylan	0.02	Norethindrone	1.00	1.00	1
Notrel	0.02	Norethindrone	1.00	1.00	1
Tarina Fe	0.02	Norethindrone acetate	1.00	1.60	2
Taytulla	0.02	Norethindrone acetate	1.00	1.60	2
Vienva	0.02	Levonorgestrel	0.10	0.83	1
Generic	0.02	Norethindrone acetate	1.00	1.60	2
Low-dose ethinylestradiol + antiandrogenic progestin					
Femilion	0.02	Desogestrel	0.15	0.51	1
Femynor	0.02	Drosperinone	3.00	0.00	1
Gianvi	0.02	Drosperinone	3.00	0.00	1
Loryna	0.02	Drosperinone	3.00	0.00	2
Micrette	0.02	Desogestrel	0.15	0.51	1
Mylan	0.02	Desogestrel	0.15	0.51	2
Mylan	0.03	Desogestrel	0.15	0.51	1
Nikki	0.02	Drosperinone	3.00	0.00	4
Viorele	0.02	Desogestrel	0.15	0.51	2
Yaz	0.02	Drosperinone	3.00	0.00	4
Generic	0.025	Norgestimate	0.35	0.67	1

Abbreviation: ; OCP, oral contraceptive pill.

unknown whether the vaginal photoplethysmograph could interfere with the measure of lubrication, lubrication and VPA were measured in response to 2 separate film presentations. Those who participate in the VPA session prior to the lubrication session were asked to gently dry their genitals with a tissue to remove any residual lubrication produced from the first film. The films were separated by a 5-minute distraction period to bring bodily arousal back to baseline. Films and order of measurement were counterbalanced. To minimize the possibility of researcher bias, the experimenters were blind to the form of OCP (ie, androgenic or antiandrogenic, if any) used by each participant. After completing both measures of sexual arousal, participants then completed the demographic and self-report surveys. At the end of the study, participants were debriefed and compensated for their time.

Data reduction

Genital sexual arousal data (ie, VPA) were exported from AcqKnowledge 3.9.3 to Microsoft Excel for processing. Movement artifacts in the data were identified and removed by an automatic processing procedure[34] that has been shown to effectively remove outliers and provide results that are comparable to visual inspection. This automatic processing procedure is conducted within the R environment (version 3.2.3; R Foundation for Statistical Computing)[35] using the MGCY[36] package for generalized additive modeling. A comprehensive explanation of this data-reduction procedure can be found elsewhere.[37] The cleaned VPA data were then binned in 5-second epochs representing mean peak-to-peak VPA response, yielding a total of 120 data points per participant.

Statistical analyses

All study analyses were conducted in R.[35] Categorical data, such as data from the clinical interviews, were analyzed using chi-square tests of independence within the MASS package for support functions and datasets for Venables and Ripley's MASS.[38] Using the corrplot package for the visualization of correlation matrices,[39] analyses of the residuals were conducted to determine the location of effects that emerged. In base R, a series of paired-samples *t* tests were conducted to determine whether each group experienced increases in lubrication from pre- to postfilm, and multivariate analyses of variance (MANOVAs) were used to test for between-group differences on measures of lubrication and self-reported vulvovaginal atrophy. Time series data (ie, VPA) were analyzed using the nlme package[40] for linear and nonlinear mixed effects. Within this, multilevel modeling was implemented to examine the extent to which participants' genital blood flow changed over time. This approach to modeling analyzes data with regards to individual growth, which is useful in this application as VPA varies from woman to woman. Multilevel modeling therefore allows for each woman to serve as her own control. Slopes and intercepts were entered as random, thus allowing them to vary across participants.[41]

Results

Presence of female sexual arousal disorder

Female sexual arousal disorder was identified in 7 (33.33%) of the women taking antiandrogenic OCPs, 12 (24.00%) of the women taking androgenic OCPs, and 5 (8.47%) of

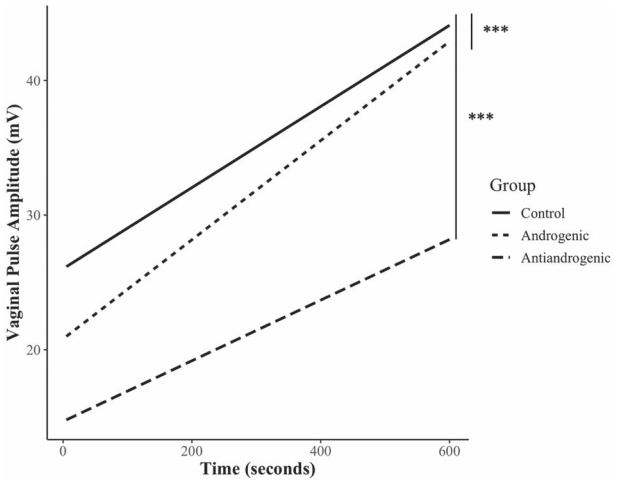

Figure 1. Linear slopes indicating vaginal blood flow over the course of an erotic film for women in the control, androgenic, and antiandrogenic groups. In this figure, vaginal pulse amplitude is measured in mV. ***$P < .001$.

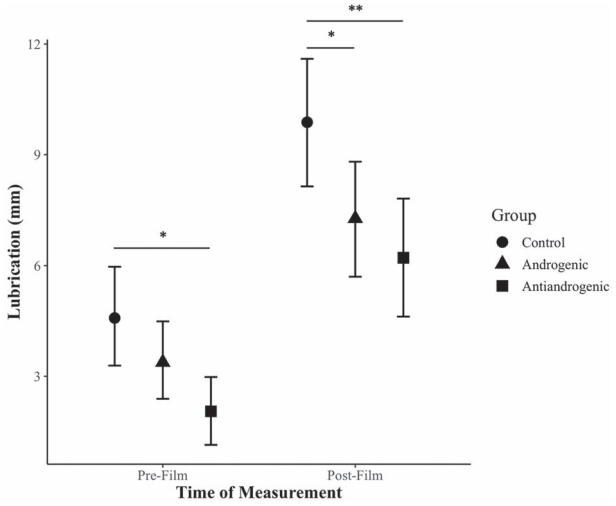

Figure 2. Antiandrogenic oral contraceptive pill (OCP) users demonstrate lower levels of prefilm vaginal lubrication. compared with androgenic OCP users and non-OCP users. All OCP users demonstrate lower levels of postfilm. lubrication compared with non-OCP users.

the women in the control group. A chi-square test of independence indicated a significant relationship between study group and the presence of female sexual arousal disorder ($\chi^2_2 = 8.013$, $P = .018$). An analysis of the residuals of the chi-square test indicated that women in the antiandrogenic group were significantly more likely, and those in the control group were significantly less likely, to meet diagnostic criteria. Despite the increased prevalence in women taking androgenic OCPs, this difference did not reach statistical significance.

As a part of the clinical interview for female sexual arousal disorder, changes in (ie, increases, no changes, decreases, or absence of) 5 prominent components of genital sexual arousal were assessed. Significantly more women in the antiandrogenic group reported decreased or absent experiences of genital lubrication compared with women in the control group (61.90% vs 8.47%; $\chi^2_2 = 24.55$, $P = .00006$). A similar pattern emerged for women in the androgenic group, though this difference was not significant (28.57% vs 8.47%). No significant differences emerged for pleasure, pulsing/throbbing, fullness/pressure/engorgement, or warmth. It, therefore, appears as though women taking antiandrogenic OCPs are most impacted by female sexual arousal disorder, and that this is driven by decreases in lubrication.

Vaginal blood flow

Significant increases in VPA over the course of the sexual films were depicted in all 3 groups of women (Figure 1). Naturally cycling women exhibited the strongest initial VPA level ($b_0 = 26.01$ mV), with a notably greater baseline compared with women taking OCPs. This was followed by women taking androgenic OCPs ($b_0 = 20.80$ mV) and then women taking antiandrogenic OCPs ($b_0 = 14.67$ mV), who displayed the weakest initial VPA level.

A moderated hierarchical linear regression found significant effects of study group on the slope of the VPA line over time for women in the androgenic and antiandrogenic groups. The slope of the VPA line for women in the androgenic group was significantly steeper, and those in the antiandrogenic group significantly weaker, than those in the control group. These results suggest the presence of a marked inhibitory effect of antiandrogenic OCPs on vaginal blood flow. Refer to Table 3 for the complete model output.

Lubrication

Significant increases in vaginal lubrication from pre- to postfilm were demonstrated in each of the 3 study groups. On average, women in the nonhormonal control group experienced a 5.28 ± 5.63 mm increase in lubrication from pre- to postfilm ($t_{58} = 7.185$, $P < .0001$). Women taking androgenic OCPs exhibited a lesser lubrication response, with an average increase of 3.89 ± 4.07 mm of lubrication ($t_{49} = 6.754$, $P < .0001$). Finally, women taking antiandrogenic OCPs exhibited an average increase of 4.16 ± 3.03 mm of vaginal lubrication ($t_{20} = 6.292$, $P = .000003$).

Results of a MANOVA identified potentially meaningful differences in lubrication scores among the 3 groups of women ($F_{2,254} = 2.254$, $P = .063$). Tukey's honest significant difference post hoc analyses revealed lower levels of baseline (ie, prefilm, unaroused) lubrication in women taking antiandrogenic OCPs compared with women in the control group ($P = .060$), as well as lower levels of postfilm lubrication (ie, aroused) in women taking androgenic ($P = .064$) and antiandrogenic ($P = .045$) OCPs compared with those in the control group. This suggests that any impact on lubrication is most notable for women taking antiandrogenic OCPs. See Figure 2 for a visualization of these results.

Self-reported vulvovaginal atrophy

Results from a chi-square test of independence indicated that women taking androgenic OCPs were significantly more likely to endorse vaginal bleeding associated with sexual activity than were women in the control group ($\chi^2_{2,130} = 9.759$, $P = .007$). Only 1 (1.69%) participant in the control group indicated they experience vaginal bleeding, whereas 10 (20%) participants in the androgenic provided positive responses. A similar phenomenon was exhibited by women in the antiandrogenic group, with 3 (14.28%) participants endorsing vaginal bleeding associated with sexual activity; however, this did not reach statistical significance. A MANOVA indicated no significant between-group differences for any of the remaining

Table 3. Moderated hierarchical regression estimates for vaginal pulse amplitude as predicted by time (level 1) and oral contraceptive pill group (level 2).

Variable	Value	SE	*df*	*t*	*P*
Intercept	26.018	3.102	15 110	8.387	.0000
Time	0.030	0.001	15 110	38.355	.0000
Androgenic	−5.212	4.562	124	−1.142	.2554
Antiandrogenic	−11.343	5.978	124	−1.897	.0601
Time × Androgenic	0.006	0.001	15 110	5.792	.0000
Time × Antiandrogenic	−0.007	0.001	15 110	−5.025	.0000

Estimates for each level 2 analysis reflect results for the stated group compared with the control group.

Vulvovaginal Atrophy Assessment items (ie, dryness, itching/irritation, dysuria, or pain) ($F_{2,250} = 1.098$, $P = .365$).

Discussion

The present study examined the effect of exogenous sex steroid hormones on women's physiological sexual arousal responses, self-reported vulvovaginal atrophy, and the presence of female sexual arousal disorder. It was hypothesized that physiological indices of sexual arousal would vary by hormonal state. Indeed, this was found to be the case. Women taking OCPs containing antiandrogenic progestins exhibited significantly lower levels of VPA and lubrication compared with women taking androgenic OCPs or women in the control group. Responses on these measures for women taking OCPs containing androgenic progestins fell between women taking antiandrogenic OCPs and women in the control group, with the control group displaying the most robust physiological sexual arousal responses. Similarly, baseline (ie, unaroused) levels of vaginal lubrication were significantly lower for women taking antiandrogenic OCPs than for women in the control group. Decrements in levels of postfilm (ie, aroused) lubrication were evidenced in women taking both forms of OCPs; women in these 2 groups had significantly lower lubrication responses compared with women in the control group. This general trend of decreased genital arousal responses in women taking OCPs is supported by recent literature reviews reporting impaired arousal responses in this population.[13–15]

The present study also investigated how OCPs with varying androgenicity may influence the presence of female sexual arousal disorder. As hypothesized, women taking antiandrogenic OCPs were significantly more likely to meet diagnostic criteria for this disorder, and decrements in lubrication seemed to drive this effect. Female sexual arousal disorder was also slightly, though not significantly, more common in women taking androgenic OCPs compared with women in the control group. These self-report data echo the objective finding that women taking any form of OCP had lower vaginal pulse amplitude and lubrication responses compared with women in the control group, though these differences were strongest for women taking antiandrogenic OCPs.

It is possible that the elevated rates of female sexual arousal disorder among OCP users is due to decreased sexual desire, which may arise in the hypoandrogenic environment induced by OCPs. Indeed, previous research indicates that the decreased levels of free and total testosterone among women taking OCPs is linked to the presence of hypoactive sexual desire disorder.[42] Additionally, several reviews of the literature on women taking OCPs suggest that decreased desire may arise as a side effect of OCP use.[13–15,22] Given that deficient sexual desire may impede the arousal response in women,[43] further research is warranted to examine the chronology of desire and arousal concerns in women taking OCPs.

Taken together, these results suggest that OCPs containing ≤25 μg ethinylestradiol negatively impact women's physiological sexual arousal responses, and this may be particularly true for OCPs containing antiandrogenic progestins. Our findings bolster previous research suggesting that the progestin component within hormonal contraceptives is highly influential in women's sexual functioning.[20,44–46] Women at risk for sexual arousal dysfunction (eg, diagnosed with diabetes, heart disease)[47] should therefore be prescribed OCPs, particularly antiandrogenic OCPs, with caution and thorough consultation of relevant sexual side effects. If women taking OCPs present with sexual arousal dysfunction, clinicians should assess the androgenicity of the pill and alter the woman's hormonal profile to allow for a greater amount of free testosterone.

One route by which clinicians may bolster free testosterone levels is through dehydroepiandrosterone supplementation, which has been previously shown to improve OCP-related sexual difficulties among women taking a drospirenone-containing OCP (ie, an antiandrogenic OCP).[48] Of note, the authors concluded that it may be necessary to completely restore women's levels of free testosterone to see significant and clinically meaningful improvements in sexual function. Alternatively, clinicians may suggest an OCP containing estradiol valerate, a synthetic, though considered natural and bioidentical, form of estrogen, or 17β-estradiol, a natural estrogen. OCPs containing these substances are less frequently prescribed in the United States compared with their synthetic counterparts. Because natural estradiol increases sex hormone binding globulin concentrations and reduces bioavailable androgens to a lesser extent than synthetic ethinylestradiol,[49] it is possible that an estradiol valerate– or 17β-estradiol–containing OCP may impact sexual arousal and overall function to a lesser extent than those that contain ethinylestradiol. For example, the estradiol valerate plus dienogest OCP has demonstrated good contraceptive efficacy[50,51] and cycle control.[52] Several studies have, in fact, found enhancing effects of the estradiol valerate plus dienogest OCP on sexual function,[46,53,54] with one study finding no difference between this OCP and an androgenic OCP containing ethinylestradiol plus levonorgestrel.[48]

The present study also examined self-reported vulvovaginal atrophy among women taking OCPs. The high rates of vaginal bleeding after sexual activity seen in the women taking OCPs are possibly due to the thinning of the vaginal tissue. There is a high density of androgen receptors within the vaginal tissue, indicating that testosterone is essential for the maintenance of healthy tissue.[55] Indeed, Labrie and colleagues[56] found that intravaginal administration of dehydroepiandrosterone facilitated an increase in superficial cells within the vagina,

as well as decreased pain associated with sexual activity. As such, it is possible that the opposite is true: reductions in androgen levels (as observed in women taking OCPs)[18] may negatively impact the vaginal epithelium. Furthermore, vaginal tissue is also responsive to estrogen. It is possible that OCP use may lead to vaginal tissue atrophy through differences in responsiveness to naturally occurring estrogen (ie, 17β-estradiol) and synthetic ethinylestradiol (a synthesis of the research examining hormones and genital tissue can be found elsewhere).[55] In other words, vaginal tissue may be more responsive to 17β-estradiol and less responsive to synthetic ethinylestradiol, thus leading to thinner vaginal tissue. Thinner tissue is more susceptible to vaginal tearing and thus bleeding[57] and may explain the increased rates of bleeding associated with sexual activity seen in the present study.

It is worth noting that the effects observed in the present study are likely conservative. In an attempt to approximate the hormonal profiles of women taking OCPs, all study sessions for naturally cycling women were conducted within the luteal phase of the menstrual cycle. However, as sexual function is closely linked to hormone expression,[4,21] aspects of women's sexual function vary across the menstrual cycle. For example, rates of sexual fantasy and desire are higher during the follicular phase compared with luteal phase,[24,27] as are sexual arousal, engagement in sexual activity, and rates of orgasm.[24–26,28] By this nature, it is likely that greater differences in sexual arousal and function would have been observed if study sessions for naturally cycling women were conducted within the follicular phase.

This research illuminated a few methodological implications for sexual psychophysiological researchers. Our findings indicate that it is critical to consider OCP use when designing and recruiting for studies of this nature as there are striking differences in VPA between women taking androgenic and antiandrogenic OCPs. Researchers within this area are urged, therefore, to carefully consider the inclusion of women taking OCPs (especially when heterogeneously included), as the stark differences in physiological responding could mask true effects within the data and lead to inaccurate conclusions. Few sexual psychophysiological studies currently control for hormonal contraceptive use despite reporting that these were used by members of the sample.[22,58,59] Furthermore, several studies failed to report whether participants were taking hormonal contraceptives altogether.[60–62] When researchers do examine potential differences in women who are and are not taking OCPs, the composition of the OCP is not always considered.[63,64] Failing to screen for this information and/or analyze separately could hinder research outcomes by obscuring true effects.

The present study has a few limitations that warrant mention. First, the majority of women who participated were heterosexual (74.61%) and college-aged (mean age = 20.12 $\pm$ 2.53 years). Though these demographic groups are the most likely to use OCPs and thus this study maps on nicely to these particular populations,[9,10] many nonheterosexual and non–college-aged women also use OCPs. The application of the results of this study to less represented populations is limited. Additionally, the lubrication test strip was self-administered. Although caution was taken when instructing participants where and how to insert the test strip to minimize between-person variability, it is possible that not all participants inserted the test strip correctly. This could have interfered with the accuracy of these particular data and potentially impacted the study results. Relatedly, though extreme efforts were taken to match the 4 erotic films for content, some women likely found certain films more arousing than others. It is possible, though unlikely, that preferences for certain settings or certain actors contributed to the observed differences in genital arousal. Additionally, our findings may lack ecological validity due to the laboratory setting in which genital sexual arousal was measured. Women in the control group likely had varying hormonal profiles, some of which may have looked similar to those of women in either of the 2 OCP groups. Though all study sessions for naturally cycling women were conducted during the luteal phase of their menstrual cycle to minimize such hormonal differences, each woman likely had different estrogen, progesterone, and androgen levels, which could have interfered with the collected data. Finally, as the presence of sexual concerns was not required for participating in the present study, we did not screen for female sexual arousal disorder during the phone screens. It is therefore impossible to assess whether there were biases in participation. It is possible that women with sexual concerns may have been more likely to participate in research assessing relationships among hormonal contraceptives and sexual arousal, and results of the present study should be interpreted with this in mind.

Nonetheless, this study is marked by a few chief strengths. Firstly, because all OCPs included in this study contained low doses of ethinylestradiol, we were able to parse apart the specific effects of the progestins on women's sexual arousal responses. Not only does this research enhance our understanding of the effects of OCPs on vaginal blood flow, a commonly examined marker of genital sexual arousal, but it also elucidates the effects of OCPs on physiological vaginal lubrication, a marker typically examined via self-report. Last, to our knowledge, this was the first study to examine variations in physiological measures of vaginal lubrication among women taking OCPs.

Conclusion

The results of the present study suggest that OCPs, particularly those containing antiandrogenic progestins, have deleterious effects on female sexual function. This was evidenced through both physiological and self-report measures. Compared with naturally cycling women, women taking OCPs had lower physiological arousal responses, and this was most pronounced in women taking OCPs containing antiandrogenic progestins. Rates of self-reported vulvovaginal atrophy, as well as female sexual arousal disorder, were also notably elevated among women taking OCPs. As naturally cycling women were assessed during the luteal phase of their menstrual cycle, our results are likely conservative estimates; more robust differences are likely to occur mid-cycle. These findings refine our understanding of the effect of sex hormones on genital tissue function, as well as the sexual side effects of various OCPs. Sexual psychophysiology researchers are urged to control for the use of oral contraceptives, as well as their androgenicity, in their research.

Author Contributions

A.B.H. (Conceptualization-Lead, Formal analysis-Lead, Methodology-Lead, Writing – original draft-Equal, Writing – review & editing-Supporting), L.N.M. (Writing – original

draft-Equal, Writing – review & editing-Lead), I.G. (Conceptualization-Supporting, Methodology-Supporting, Writing – review & editing-Supporting), C.M.M. (Conceptualization-Supporting, Methodology-Supporting, Writing – original draft-Supporting, Writing – review & editing-Supporting).

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