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Article

Do Sex Hormones Influence the Helmholtz-Kohlrausch Effect?

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Abstract: Saturated lights appear brighter than white lights of the same luminance. This phenomenon is known as the Helmholtz-Kohlrausch (H-K) effect and can be estimated by modeling achromatic luminance and saturation to total brightness. These models have been shown to differ between women and men and are more variable in women. The variation in brightness models among women may be due to hormonal changes across the menstrual cycle. To test this, total brightness (B) and achromatic luminance (L) were measured across blue, green, yellow-green, yellow, and red hues. These data were measured along with salivary hormone levels for nine cycling women at points representing the menstrual, peri-ovulation, and luteal phases. These data were also collected for seven oral contraceptive (OC) users. OC use nor menstrual cycle phase had no main effects on B/L ratios, but ratios were higher for the red stimulus in cycling women than OC users. Red B/L ratios were also higher for cycling women than OC users during the luteal phase. Estrogen, progesterone, and their interaction predicted 18% of the variation in brightness for cycling women. These models could not be fit for OC users, and estrogen only accounted for 5% of brightness variance with progesterone terms omitted. These findings and potential mechanisms are discussed in the context of previous results.

Keywords: Helmholtz-Kohlrausch effect; luminance; brightness; saturation; contraception; menstrual cycle; hormones

1. Introduction

There is robust evidence suggesting that female visual systems are better tuned for chromatic stimuli [1,2]. Specific support for this difference comes from studies of saturation [3-5], contrast thresholds of stimuli biased towards separate parallel pathways [6], sorting colored caps [7], and duration of color afterimages [8,9]. There is growing evidence of genetic mechanisms that produce gender dimorphism independent of sex hormones [10], and it would be a gross error to fully attribute sex differences in the human visual system to circulating sex steroid hormones or the menstrual cycle [11]. There are a few reports of menstrual cycle effects on color perception which are equivocal but interesting. Finkelstein found restricted chromatic visual fields and a shift in the position of unique green (toward yellow) during the menstrual phase [12]. Lorenzetti also found constricted visual fields to red and green stimuli with decreased green and yellow sensitivity during the menstrual phase [13]. Other studies have demonstrated that standard achromatic visual fields do not vary across the menstrual cycle [14-16], but two of these studies have linked the menstrual cycle to chromatic visual field changes and suggested decreased sensitivity to blue stimuli during the high estrogen and high progesterone luteal phase [14,15]. A study of cyclical effects on isolated short-, medium-, and long-wavelength sensitive (i.e., blue, green, and red cone) photoreceptor mechanisms revealed cyclical effects for blue, but less so for green and red [17]. Color discrimination has been found to be best near ovulation [18], but a more recent study of the speed of color judgments revealed that the fastest reactions to non-cognitive blue and yellow stimuli during the menstrual phase [19].

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The perceptual attributes of self-luminant color objects are brightness, hue (name of the color), and saturation (colorfulness as a proportion of an object's brightness). The perception of a colored object occurs via two anatomically and functionally distinct magnocellular and parvocellular parallel pathways and is complex [20]. Fortunately, these contributions can be quantified by methods such as heterochromatic flicker (HFM) and direct brightness (DBM) matches.

HFM involves minimizing perceived flicker when alternating a test light against a spatially matched reference light. The visual system produces a luminance signal for each color by linear addition of long- and medium-wavelength-sensitive cone photoreceptor contributions [21]. An observer adjusts the intensity to minimize flicker perception, and the relative luminosity is calculated for each color as the ratio of the reference luminance to that of the color stimulus. If the flicker rate is fast enough, contributions from the slower chromatic channels are avoided, and equally luminous flickering stimuli will appear to be continuous. Typical flicker rates for HFM are 18-25 Hz [22]. HFM measures are used to form standard luminous efficiency functions used in calibrating visual displays because they are additive. That is, the luminance of a mixture of colors A and B should be equal to the sum of luminance A and luminance B [21].

Direct brightness matches (DBM) are not additive. During DBM, an observer adjusts the intensity of the color field until it matches in brightness to the reference field. Although it seems simple, DBM is more difficult and less repeatable than HFM for most observers [23]. Paradoxically, additivity failures from the contribution of chromatic channels enhance brightness. This is even more so for more saturated short (blue) or long (red) wavelengths [24]. Brightness is less enhanced in less saturated (i.e., whiter) colors or combinations of colors such as yellow or yellow-green. This complex effect of saturation on perceived brightness is known as the Helmholtz-Kohlrausch (H-K) effect [25] (Figure 1).

Figure 1. The Helmholtz-Kohlrausch effect. The colored patches loosely represent the blue, green, yellow-green, yellow, and red used in the current experiment. They are converted to greyscale and have the same luminance as the background (depending on monitor calibration). For most observers, blue and red will be the brightest, followed by green, then yellow-green or yellow will be the dimmest.

A simple explanation of the Helmholtz-Kohlrausch effect is that lights containing colors appear brighter than white lights of the same luminance, and the effect has been shown both theoretically and experimentally to be derived from the ratio of chromatic to achromatic activation [26]. A recent investigation using simple ratios of perceived total brightness (via DBM) to perceived achromatic luminance (via HFM) revealed a clear but small (0.25-0.37 log unit) female advantage in the effect [3]. However, to best understand the H-K effect, one needs to understand that the brightness-luminance relationship is non-linear and varies according to: $B = aLn + b$, where B is brightness, L = luminance, and a, b, & n are constants [27]. More recent models propose that brightness also varies with changes in chromaticity according to: $B = L^a 10^c$, where a = coefficient for achromatic contribution, and c = coefficient for chromatic adaptation (adapted from Sagawa [28]). The logarithmic form of this equation becomes $log(B) = a\ log(L) + c$. As the H-K effect is based on saturation [26], Foutch and Bassi proposed an additional saturation term in the model, arriving at: $log\ B = a_0 + a_1 logL + a_2 S_\lambda$, where a_0 = constant for regression model, and a_1, a_2 are the coefficients for achromatic luminance and saturation, respectively [3]. This model allowed for brightness to depend on both luminance and saturation without constricting the coefficient for luminance (a_1) to 1.0 as is done in simple B/L ratio approximations of the H-K effect.

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The H-K effect has been shown to vary greatly between individuals [3,26], which could implicate hormonal changes associated with the menstrual cycle. Foutch and Bassi further revealed that the coefficient for the saturation term in brightness models was larger in women than men (0.649 vs. 0.480) and that saturation predicted more variance in perceived brightness in women (9%) than in males (5%)[3]. However, the overall model predicted 61% of brightness for men but only 48% for women. Therefore, while models of the H-K effect are gender dimorphic, the decreased fit of the model for women suggests a within-females variation that may be associated with cyclical and/or hormonal changes. The steroid sex hormone estrogen has significant effects on human physiology outside of reproduction [29], and estrogen receptor (ER) proteins have been observed in both male and female ocular structures [30,31]. Progesterone receptors have also been localized in mammalian retinas [32]. Endogenous sex hormone levels vary predictably across the menstrual cycle [33] but can be exogenously modulated with selective estrogen receptor modulators (SERMs; often used as adjuvant therapies for breast cancers) or more commonly with oral contraceptives (OC), both of which have been associated with changes in color perception [34-37].

There are three types of endogenous estrogens, but the primary form produced during reproductive ages is 17β-estradiol (referred to here as estradiol or E2). There are large perturbations in estradiol and progesterone (P) levels during the female menstrual cycle. An idealized menstrual cycle lasts approximately 28 days and can be divided into follicular (days 1-14; low E2, low P levels) and luteal (days 15-28; high E2, high P levels) phases [38]. The follicular phase can be further divided into the menstrual (days 1-7 at the beginning of the cycle; low E2, low P levels) and late follicular (days 7-14; increased E2 but low P levels) phases. At the midpoint of the cycle is the peri-ovulatory phase (~day 13; preceded by a first E2 peak but low P levels). Understanding this pattern allows researchers to assume categorical E2 and P levels when examining their effects on perception or behavior [33,39].

That is the purpose of the current follow-up investigation; to determine whether the Helmholtz-Kohlrausch effect is higher in cycling women and during phases of the menstrual cycle when hormone levels are higher.

2. Materials and Methods

2.1. Subjects

An a priori power analysis was based on a relatively small effect size ($\eta^2 = .27$) found in a previous study of OC effects on B/L ratios [3]. To achieve a power (1-β) of 0.80, a significance level (α) of .05, and a fixed factor with two groups (cycling women vs. OC users), 19 participants were needed. Subjects were eligible if they were between 18 and 45 years old, had best-corrected visual acuity of 20/20 or better in each eye, and had normal color vision with psuedoisochromatic plates and the Nagel anomaloscope. Subjects were ineligible if they were currently pregnant, unwilling to share the starting date of their current menstrual cycle or were menopausal. In addition, any history of neurological or psychiatric conditions, medication or nutritional supplement use known to affect color vision, or a family history of color defective vision was also disqualifying. Hormonal contraceptive use was permissible. The institutional review board of the University of Missouri –St. Louis approved the experimental protocol, and informed consent was obtained from 19 women. Three women decided to withdraw based on scheduling conflicts. Of the 16 women (ages 21-40 years) willing to provide the date of the first day of menses for their current menstrual cycle, nine participants were experiencing normal cycles (ages 25.8 ± 3.2 years) and seven were using combination oral contraceptives containing progesterone and estrogen compounds (ages 26.0 ± 6.2 years).

2.2. Sessions

Sessions were scheduled during the menstrual (days 1-7), peri-ovulation (~day 12), and luteal (~day 21) phases. Menstrual phase sessions were scheduled within five days of

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the start of menses. It is well established that the length of the typical luteal phase is 14 days, but the length of the follicular phase varies a great deal between women [40]. It has also been shown that peak estrogen levels occur 24-36 hours prior to ovulation or 16 days prior to the start of the next cycle [38]. Ovulatory and luteal sessions were then scheduled to occur 16 and seven days, respectively, before the projected start of the next cycle. If an experimental session was not completed within three days of a predicted marker, that session was rescheduled during the second month. The same scheduling process was used for all participants. Although OC users do not experience monthly hormonal cycles, data were collected at similar times (i.e., days 1-8, ~day 12, ~day 21) and served as observational controls. Four subjects (three cycling women and one OC user) only completed sessions during the menstrual and luteal phases during the data collection window.

2.3. Data Collection

2.3.1. Hormone measures

All participants were provided three saliva collection kits (ZRT Laboratory, Beaverton, OR). Participants collected saliva samples at home on the day of each experimental session prior to eating, drinking, or brushing their teeth. The collected samples were brought to each session and were mailed the day they were received. Progesterone was measured with a direct competitive radioimmunoassay (RIA), while estradiol was measured by double antibody RIA.

2.3.2. Apparatus

A three-channel open-view optical system was used to produce a 2.5-degree, circular field for both experimental tasks. A uniform circular field was used for heterochromatic flicker measures (HFM), while a side-by-side bipartite field was used for direct brightness measures (DBM). A computer-controlled narrow bandpass interference filter (NBIF) wheel produced each of the five test wavelengths. The second channel was a spectrally broad reference channel that was split into two channels via a front surface mirror translated in and out of the reference beam. With the mirror in place for the HFM task, the test and reference beams were spatially merged but temporally separated via a mirrored optical chopper rotating at 18 cycles/sec (Hz) and alternately illuminated the frosted end of an acrylic cylinder. The opposite end of the cylinder served as a 1.9 cm diffuse circular viewing screen. For the DBM task, the reference beam was reflected onto the left viewing half of a bipartite viewing field, separated from the color test field by a 0.5 mm-thick aluminum sheet. A chin rest was used to position the observer 43 cm from the viewing end of the optic viewed by the right eye.

2.3.3. Procedure

Prior to each experimental session, task order (HFM or DBM) and wavelength presentation was randomly generated. Each session began for each participant by adapting to a background room luminance (~ 0.4 cd/m^2) for approximately five minutes. Participants then practiced matches while a Xenon bulb was allowed to warm up for at least thirty minutes. During practice, a minimum of four trials were performed at each test wavelength—450, 520, 560, 580 and 650 nm—for both HFM and DBM tasks. This process was repeated until the subject was successful at making reliable sets of matches (i.e., the range of trials at each wavelength fell within one standard deviation of the mean at all five test wavelengths) for both methods.

Before each set of trials, the subject adapted for thirty seconds to a broadband reference stimulus. After adapting to the reference field, participants adjusted the intensity of the test stimulus until it matched the reference field (for DBM) or minimized the flicker sensation (for HFM). The test stimulus intensity value was automatically decreased by 1-2 log units. Four trials were completed in succession at each wavelength, followed by another thirty-second adaptation period. This process was repeated for all five wavelengths for both tasks.

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2.4. Data Analysis

The luminance values for the four trials at each wavelength were averaged. Relative luminosity (RL) at each wavelength was calculated by dividing the reference stimulus luminance (5 cd/m^2) by this average. RL values from the DBM task were used as estimates of total brightness (i.e., chromatic + achromatic activation), indicated further here by the letter B. RL values from the HFM task were used as estimates of perceived luminance (i.e., achromatic activation) which will be represented by the letter L. For regression models, saturation was calculated as $S_\lambda = 13([u_n\text{-}u'_n]^2 - [v_n\text{-}v'_n]^2)^{1/2}$, where (u_n,v_n) and (u'_n,v'_n) are the chromaticity values of the color and reference broadband stimuli, respectively, in CIELUV space. The normalized saturation values of the current stimuli were: 1.00 (blue at 450 nm), 0.60 (green at 520 nm), 0.31 (yellow-green at 560 nm), 0.29 (yellow at 580 nm), and 0.99 (red at 650 nm).

All variables were analyzed for normality using Kolmogorov-Smirnov tests. Plots of salivary estradiol and progesterone across the menstrual phase were then visually compared with established laboratory reference values (Figure 2). Repeated measures (RM) analysis of variance (ANOVA) was used to compare the within-subjects effects of menstrual cycle (MC) phase and between-subjects effects of OC use on estradiol levels. RM ANOVA was then performed to determine the within-subjects effects of MC phase on estradiol levels with OC use as a fixed between-subjects factor. Reduced number of successful progesterone assays constrained the analysis to univariate ANOVA with OC use and MC phase as fixed effects. Repeated measures ANOVA was used to determine the between-subjects effects of OC use and within-subjects effects of MC phase on B/L ratios. Post-hoc comparisons were used to determine pairwise differences in hormone levels and B/L ratios between menstrual, peri-ovulation, and luteal phases. Post-hoc paired comparisons of B/L ratios between cycling women and OC users were also performed for all five hues across the three menstrual cycle phases.

Lastly, estradiol and progesterone terms were added to the regression model to determine their influence on the H-K effect, arriving at: $log(B) = a_0 + a_1log(L) + a_2S_\lambda + a_3(E2) + a_4(P) + a_5(E2 \times P)$, where $E2$ = salivary estradiol and P = salivary progesterone. The additional hormone terms were also regressed onto brightness for all participants then for cycling women and OC users separately. All statistical analyses were performed using SPSS for Windows (SPSS Inc., Chicago, IL) and R (R Programming Language, Free Software Foundation, Boston, MA).

3. Results

3.1. Salivary estradiol and progesterone levels

Data collection took place on the following (M ± SD) days for cycling women: menstrual (3.7 ± 2.0), peri-ovulation (11.5 ± 0.8), and luteal (19.7 ± 1.6) and OC users: menstrual (4.0 ± 2.8), peri-ovulation (11.8 ± 1.8), and luteal (19.4 ± 1.5). Kolmogorov-Smirnov tests revealed that neither raw estradiol ($p = .009$) nor progesterone measures ($p = .046$) were normally distributed. Log-transformed estradiol ($p = .200$) and progesterone ($p = .564$) levels were normally distributed and used for all subsequent analyses.

Figure 2 shows individual estradiol and progesterone values for cycling women and OC users across menstrual cycle phases. Most estradiol levels were lower than reference saliva ranges (www.zrtlab.com/resources/reference-documents/saliva-reference-ranges) for cycling women during the menstrual phase and peri-ovulation. Progesterone levels were lower than reference ranges for cycling women during the luteal phase. Estradiol and progesterone levels were within reference ranges for OC users.

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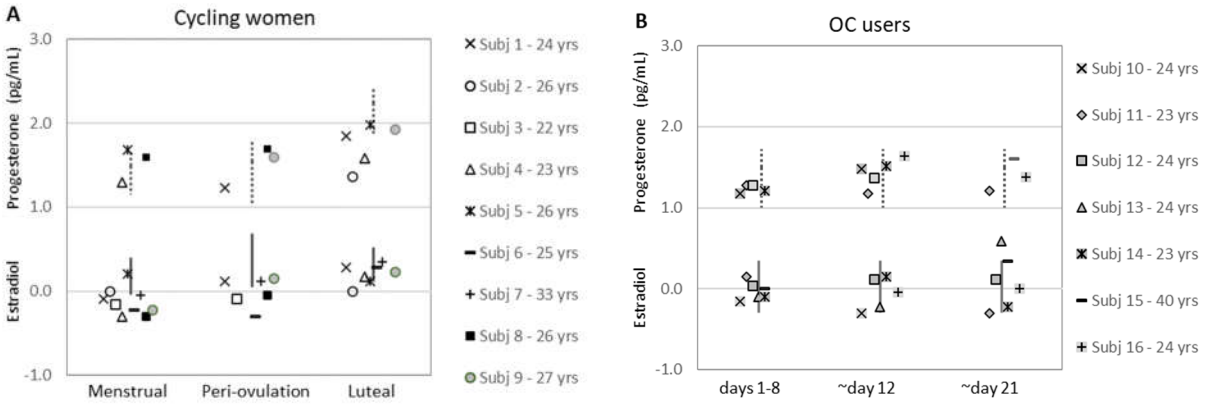

Figure 2. Logarithmic salivary estradiol and progesterone levels across the menstrual cycle plotted separately for cycling women (A) and oral contraceptive users (B). The vertical bars represent reference hormone ranges for estradiol (solid) and progesterone (dotted). (Subject numbers are arbitrary here for the manuscript and do not represent assigned subject identities.).

Mean estradiol levels were equivalent between cycling women and OC users ($F[1,7] = 0.49$, $p = .507$, $\eta^2 = .065$). Estradiol levels did vary significantly across MC phases for all participants ($F[2,14] = 5.68$, $p = .016$, $\eta^2 = .45$) and were higher on pairwise comparisons during the luteal phase than the menstrual phase for all women ($t[16] = 3.88$, $p = .003$). For cycling women, estradiol levels were also different across MC phases ($F[2,8] = 13.01$, $p = .003$, $\eta^2 = .77$), where luteal levels were higher than menstrual phase levels ($t[8] = 7.10$, $p < .001$). Estradiol levels were not different between MC phases for OC users ($F[12,6] = 0.713$, $p = .519$, $\eta^2 = .20$) nor were there any pairwise differences between the three phases.

Progesterone levels were higher for cycling women ($F[1,18] = 10.31$, $p < .001$, $\eta^2 = .19$) but were the same across all three phases for all participants ($F[2,18] = 2.06$, $p = .157$, $\eta^2 = .19$), cycling women ($F[2,12] = 1.81$, $p = .214$, $\eta^2 = .29$), and OC users ($F[2,9] = 2.00$, $p = .191$, $\eta^2 = .31$). Luteal levels were higher than during the menstrual phase ($t[13] = 2.18$, $p = .05$) for all participants, but there were no pairwise progesterone differences across MC phases for cycling women or OC users separately.

3.2. Effects of contraception and menstrual cycle phase on B/L ratios

Plots of B/L ratios for all participants across wavelength by OC use and menstrual cycle phase are shown separately in Figure 3. B/L ratios were slightly higher for cycling women than OC users, but the difference did not reach significance ($F[1,10] = 1.83$, $p = .206$, $\eta^2 = .16$; see Figure 3A).

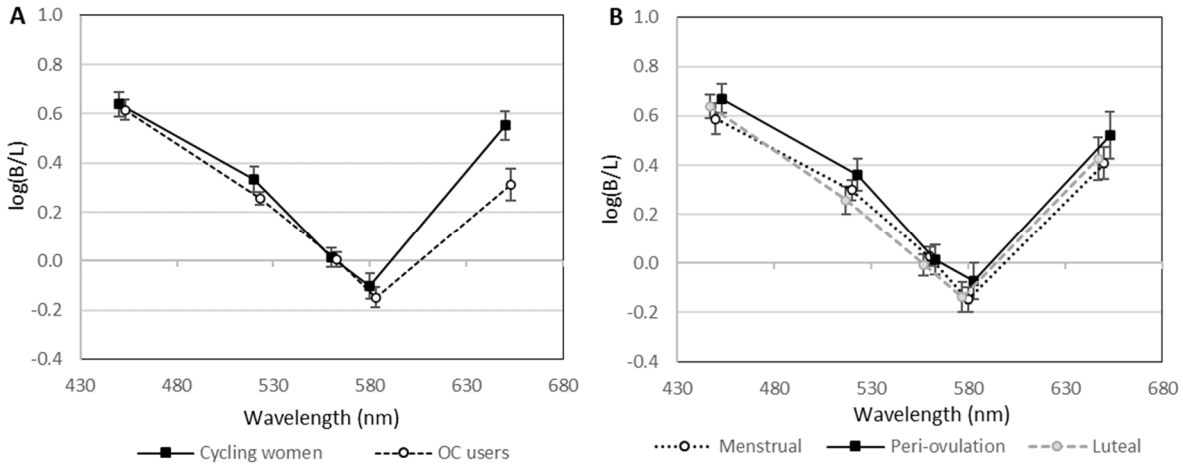

Figure 3. Mean B/L ratios for all participants by OC use (A) and menstrual cycle phase (B). Error bars = ±1 SEM.

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On visual inspection of Figure 3A, B/L ratios were much higher at 650 nm for cycling women than OC users at 650 nm. This difference was confirmed on pairwise comparisons ($t[43] = 2.73$, $p = .009$). There were no main within-subjects effects of MC phase ($F[2,20] = 2.01$, $p = .160$, $\eta^2 = .17$; see Figure 3B). B/L ratios appeared higher during peri-ovulation than other phases, but there were no statistically significant pairwise differences for all participants between phases (Figure 3B). B/L ratios for cycling women and OC users separately are shown in Figure 4. There were no main within-subjects effects of MC phase for cycling women ($F[2,10] = 1.18$, $p = .347$, $\eta^2 = .19$; see Figure 4A) nor OC users ($F[2,10] = 2.00$, $p = .186$, $\eta^2 = .29$; see Figure 4B). On visual inspection, B/L ratios were lowest for cycling women during the (low hormone) menstrual phase for the 450 and 650 nm stimuli. However, there were no pairwise differences between phases for cycling women.

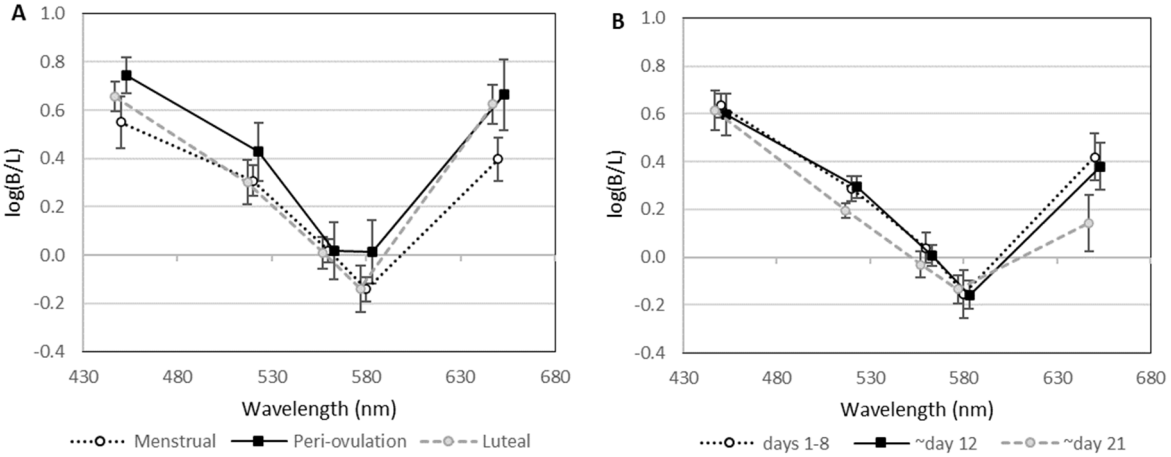

Figure 4. Mean B/L ratios for cycling women (A) and OC users (B). Error bars = ±1 SEM.

For OC users, B/L were depressed around day 21 compared to other "phases" (see Figure 4B), but the differences were not significant on pairwise testing. There was a strong trend toward lower B/L ratios around day 21 compared to days 1-8 at 650 nm ($t[10] = 2.05$, $p = .075$). Lastly, there was an interaction effect of OC use and MC phase at 650 nm where B/L ratios were higher for cycling women during the luteal phase than for OC users around day 21 ($t[10] = 2.70$, $p = .022$).

3.3. Regression models of estradiol and progesterone on B/L ratios

Linear regressions were calculated to predict total brightness (B) based on luminance (L), saturation (S_λ), estradiol (E2), and progesterone (P) separately for all participants. The regressions were performed stepwise to determine the effects of luminance, saturation, then hormone levels (see Table 1). The luminance only model (i.e., $B = a_0 + a_1 logL$) was significant but only predicted 29% of the variance in brightness. Adding saturation (S_λ) to the regression model resulted in 22% of additional predicted variance (i.e., ΔR^2). Adding the hormone terms (logE2, logP, logE2 x logP) resulted in an ΔR^2 of .08 and an overall significant regression equation ($F[5,114] = 36.5$, $p < .001$, $R^2 = .59$). These results along with the regression coefficients are summarized in Table 1.

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Table 1. Regression results for all participants using brightness (B) as the criterion.

Predictors	*Coefficient*[d]	*SE*	*95% CI*		*p*	*Model fit*	*Fit difference*
			LL	*UL*			
(constant, a_0)	-0.76	0.14	-1.04	-0.47	<.001	--	--
Luminance (logL)[a]	1.07	0.10	0.89	1.26	<.001	R^2 = .29***	--
Saturation (S_λ)[b]	1.04	0.12	0.79	1.28	<.001	R^2 = .51***	ΔR^2 = .22
Estradiol (logE2)	3.50	0.75	2.02	4.97	<.001	--	--
Progesterone (logP)	0.28	0.10	0.09	0.47	.004	--	--
Inter.(logE2 x logP)[c]	-2.40	0.50	-3.38	-1.42	<.001	R^2 = .59***	ΔR^2 = .08

Note. CI = confidence interval; LL = lower limit; UL = upper limit. [a] Predictors: (Constant), log(L). [b] Predictors: (Constant), log(L), saturation. [c] Predictors: (Constant), log(L), saturation, logE2, logP, logE2 x logP. [d] Coefficients for model containing all terms. *** p < .001.

For cycling women, all models were also significant (see Table 2). The luminance only model only predicted 18% of the variance in B and adding saturation to the regression model resulted in a total R^2 of .55 (ΔR^2 of .37). Adding the hormone terms resulted in an ΔR^2 of .18 and an overall significant regression equation ($F[5,59] = 27.0$, $p < .001$, $R^2 = .73$). These results along with the regression coefficients are summarized in Table 2.

Table 2. Regression results for cycling women using brightness (B) as the criterion.

Predictors	*Coefficient*[d]	*SE*	*95% CI*		*p*	*Model fit*	*Fit difference*
			LL	*UL*			
(constant, a_0)	-1.13	0.20	-1.52	-0.73	<.001	--	--
Luminance (logL)[a]	1.07	0.13	0.82	1.31	<.001	R^2 = .18***	--
Saturation (S_λ)[b]	1.13	0.16	0.82	1.44	<.001	R^2 = .55***	ΔR^2 = .37
Estradiol (logE2)	5.19	1.04	3.16	7.23	<.001	--	--
Progesterone (logP)	0.52	0.13	0.26	0.77	<.001	--	--
Inter.(logE2 x logP)[c]	-3.66	0.68	-4.98	-2.34	<.001	R^2 = .73***	ΔR^2 = .18

Note. CI = confidence interval; LL = lower limit; UL = upper limit. [a] Predictors: (Constant), log(L). [b] Predictors: (Constant), log(L), saturation. [c] Predictors: (Constant), log(L), saturation, logE2, logP, logE2 x logP. [d] Coefficients for model containing all terms. *** p < .001.

The results were different for OC users. The luminance only model was significant and predicted a much higher portion (48%) of the variance in brightness than for cycling women. Adding saturation to the regression model only resulted in a total R^2 of 59% (ΔR^2 = .11). When adding all the hormone terms to the model, the constant coefficient (a_0) and coefficients for the hormone terms were not significant. When adding E2, P, and the interaction term stepwise individually, a significant regression equation was found for luminance, saturation, and E2 ($F[3,51] = 26.0$, $p < .001$, $R^2 = .64$). Adding E2 to the regression model only resulted in a ΔR^2 of 5%. The results for the significant models in OC users are summarized in Table 3. Modeled B/L ratios for cycling women and OC users are plotted along with observed values in Figure 5.

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Table 3. Regression results for OC users using brightness (B) as the criterion.

Predictors	*Coefficient*[d]	*SE*	*95% CI*		*p*	*Model fit*	*Fit difference*
			LL	*UL*			
(constant, a_0)	-0.28	0.06	-0.40	-0.15	<.001	--	--
Luminance (logL)[a]	0.90	0.13	0.64	1.16	<.001	R^2 = .48***	--
Saturation (S_λ)[b]	0.69	0.19	0.32	1.05	<.001	R^2 = .59***	ΔR^2 = .11
Estradiol (logE2)[c]	0.34	0.14	0.08	0.61	.014	R^2 = .64***	ΔR^2 = .05

Note. CI = confidence interval; LL = lower limit; UL = upper limit. [a] Predictors: (Constant), log(L). [b] Predictors: (Constant), log(L), saturation. [c] Predictors: (Constant), log(L), saturation, logE2. [d] Coefficients for model containing all terms. *** p < .001.

4. Discussion

4.1. Notable results

The most notable finding of the present study is that brightness models differed between cycling women and OC users (Figure 5). In cycling women, luminance, and hormone terms each predicted 18% while saturation predicted 37% of the variance in brightness. This contrasts with OC users, where luminance predicted 48% and saturation only predicted 11% of the variance in brightness. Estradiol only predicted ~5% of brightness in OC users, and progesterone could not be successfully modeled to brightness. B/L ratios for cycling women from models including saturation and/or luminance slightly underestimated observed ratios (see Figure 5A), but they more closely aligned to observed ratios than data modeled for OC users (Figure 5B). The only stimulus modeled better for OC users was yellow-green (560 nm). This is not so surprising, as the models in OC users rely more heavily on luminance, and the peak luminous efficiency for most observers is near 560 nm [21].

While the differences between cycling women and OC users represent small (threshold level) differences in modeled brightness, these results build on previous results that found clinically relevant threshold level differences in chromatic stimuli across the menstrual cycle [14] and for modulated estradiol [35].

The second notable finding can be seen in Figure 3A, where B/L ratios were slightly higher for cycling women across all stimuli but significantly higher at 650 nm. This finding (p = .009) for the red (650 nm) stimulus survives a conservative Bonferroni post-hoc correction for five comparisons (adjusted p = .045) and represents a large effect (Cohen's d = 0.82). There were no such B/L differences for the red stimulus in a previous study by the present author [3]. However, that study compared cycling women in a random phase of the menstrual cycle with OC users also at random days. In the present study, data for cycling women were systematically collected and compared from all phases and compared with data from OC users. When doing so, the lowest B/L ratios at 650 nm for cycling women during the menstrual phase (see Figure 4A). This implicates estradiol, which was lowest during the menstrual phase for cycling women (see Figure 2A). B/L ratios were lowest for OC users during the luteal phase (see Figure 4B) when estradiol and progesterone levels were lower than in cycling women (Figure 2B). The clear interaction of luteal phase and OC use further implicates progesterone in the difference for the red stimulus.

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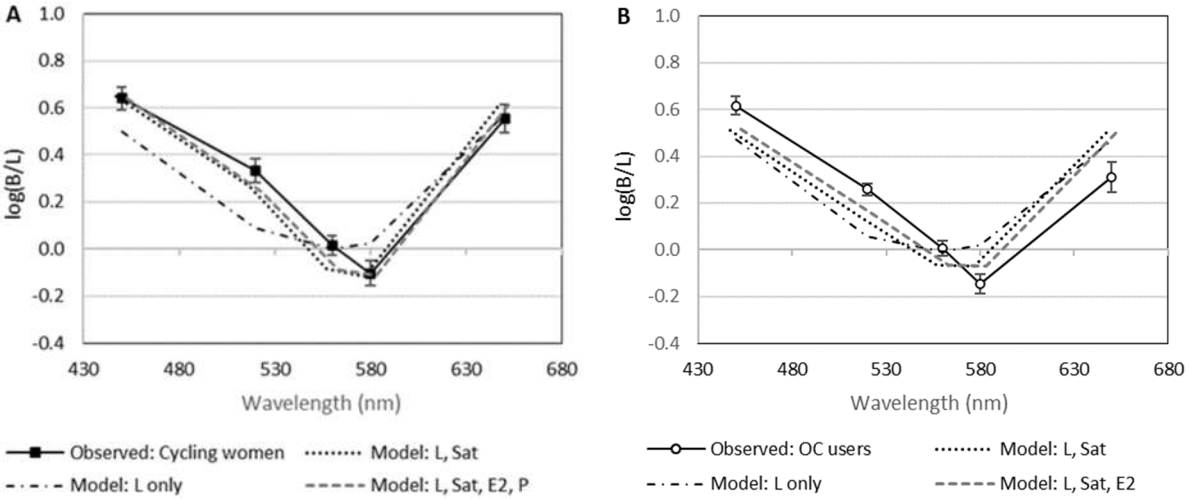

Figure 5. Observed and modeled B/L ratios for cycling women (A) and OC users (B). Error bars = ±1 SEM.

While E2 and P were highest in the present study in cycling women during the luteal phase, B/L ratios were highest in cycling women during peri-ovulation. This contrasts with a similar study that compared the hue ordering of saturated color caps with desaturated, more luminous caps [41]. They found the agreement to be worse (i.e., saturation mattered most) during the third trimester in pregnancy, when estrogen peaks. Giuffrè et al. [18] also found that color discrimination was highest near ovulation, where estrogen peaks. These and the present result may be explained by factors outside the direct influence of ovarian hormones. Pregnancy is a vastly different physiological state, and the elevated E2 and P levels of the luteal phase in cycling women may be offset by a physiologically stressed anabolic state where nutrients (e.g., amino acids) are being over-utilized to prepare for pregnancy [42]. The synergism of elevated E2 and P levels also causes a slight increase in basal body temperature during the luteal phase [43]. However, the goal of most hormonal contraceptive devices is to inhibit ovulation. When ovulation does not occur, the corpus luteum decays and stops secreting progesterone [39]. So, in a sense, if contraception is successful, there is no luteal (or any other) "phase" in most OC users, and the present B/L ratio differences between cycling women and OC users during the luteal phase can be explained by other physiological effects.

For example, de Vries demonstrated that a 1-degree increase in core body temperature increased an observer's threshold sensitivity to 660 nm (i.e., red) light [44]. St. George also concluded that visible sensations to red stimuli depended on temperature as well as stimulus lightness [45]. While only loosely associated with the current task, Kim and Tokura used color chips and found that redder colors were preferred over blue and green colors during the luteal phase [46]. Participants' temperature was not measured in the present study, so this remains an interesting topic of future inquiry. Increased ionic absorption increases cone photoreceptor excitation [47], leading to increased neurotransmitter release and enhanced probability of a visual signal. Knowles found that the relative absorption of red light in chicken photoreceptors increased as serum concentrations of chloride ion increased [48]. Venkatesh et al. further suggested that ion level changes during the menstrual cycle could affect visual sensitivity [49]. At least one study has found that estrogen decreased blood flow resistance and was beneficial to ocular hemodynamics [50]. Others have investigated the effects of blood flow on the suppression of long-wavelength (i.e., red) cone responses to a very intense 640 nm stimulus and found that flicker suppression was related to heart rate but inversely related to blood pressure [51]. It is possible then to attribute a portion of the present difference in B/L ratios for the red stimulus to either cyclical temperature, ionic, or blood flow changes that occur in cycling women but not contraceptive users.

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While the present effects of hormonal contraception and menstrual cycle phase for the red stimulus are interesting, the absence of effects for the blue stimulus are surprising. The blue stimulus was the most saturated of the stimuli, and B/L ratios are approximations of the H-K effect which depend on saturation. In addition, the balance of previous hormonal effects are for short-wavelength stimuli [14,15,35]. While unplanned, it was then useful to examine simple bivariate correlations between hormone levels (estradiol, progesterone, or their interaction) and B/L ratios at each wavelength. There were no significant bivariate relationships between B/L ratios and estradiol or progesterone. The only significant finding was for OC users where ratios at 450 nm were positively correlated with the interaction of E2 x P ($r = .681$, $p = .021$). This is a challenging result to interpret. Correlations between B/L ratios and E2 x P were negative for all stimuli for cycling women (range [-.368, -.026]; $p > .05$), which compares with previous results that implicate high E2 and P levels (during the luteal phase) in decreased sensitive to short-wavelength stimuli during visual field testing [14,15]. However, correlations were positive for the present OC users (range [.314, .681]; significantly for the 450 nm stimulus), contrasting with previous results. While the mean (± SD) log(E2 x P) levels were higher in cycling women (1.70 ± 0.36) than in OC users (1.36 ± 0.30), that cannot explain the opposite signs of these correlations. It is more logical and likely that the visual mechanisms transforming short-wavelength stimuli react differently to the synergism of estradiol and progesterone during the triphasic menstrual cycle than during the monophasic state of OC users.

The present relationship between B/L ratios at 450 nm and estradiol in HC users may be related to previous reports of differences in the color naming of a short-wavelength stimulus which find that about 1/3 of healthy women described a short-wavelength (440 nm) patch as "white" more often than "blue" or "lavender" [35]. In addition, most subjects using estrogen modulator therapy also referred to the patch as "white" more often than peri- or post-menopausal middle-aged control subjects not using any hormonal therapies. The experimental dynamics of that study were vastly different from the current study, using a threshold level "blue" stimulus against an adaptive yellow background, but the present study examined luminosity of supra-threshold test stimuli in young, pre-menopausal participants. However, the present findings are related to and add to the body of evidence for hormonal effects for short wavelength stimuli.

4.3. Reliability of findings

B/L data for all subjects are plotted in Figure 6. There is certainly between-subject variability in B/L ratios, especially with respect to the small number of participants. However, it is clear from Figure 6 that the variation is greater in cycling women. This is most evident when comparing cycling women in peri-ovulation and luteal (i.e., higher hormone phases) with OC users in similar days of their "cycle" (e.g., compare Figure 6B with 6E).

Further, while the direct relationships between B/L ratios and hormone levels were limited, the increased variability in B/L ratios among cycling women is comitant with an increased variability in estradiol and progesterone levels (see Figure 2).

The B in the B/L ratios is derived from DBM measures which have long been known to be "uncertain…" to observers, and this difficulty becomes enhanced when the stimuli are less similar [52]. This was reported by some of the present participants who saw a "glow" when viewing the blue and red stimuli, referred to in early descriptions of the H-K effect as "Farbenglut" or "color glow" [53]. So, ironically, matches for the highly saturated stimuli (i.e., blue and red) are the most difficult, but they produce the largest H-K effect. Previous authors have used a similar method of adjustments to that used in the current report and found similar DBM "noise" [54]. Attempts were made to control for using the method of adjustments by first adapting subjects to a very low background room luminance then allowing them to practice for 30 minutes. Practice sessions were monitored, and participants needed to demonstrate consistent flicker and direct matches at

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each wavelength before starting the experimental sessions. In addition, brightness "expectations" were controlled by randomly resetting the color intensity after each trial.

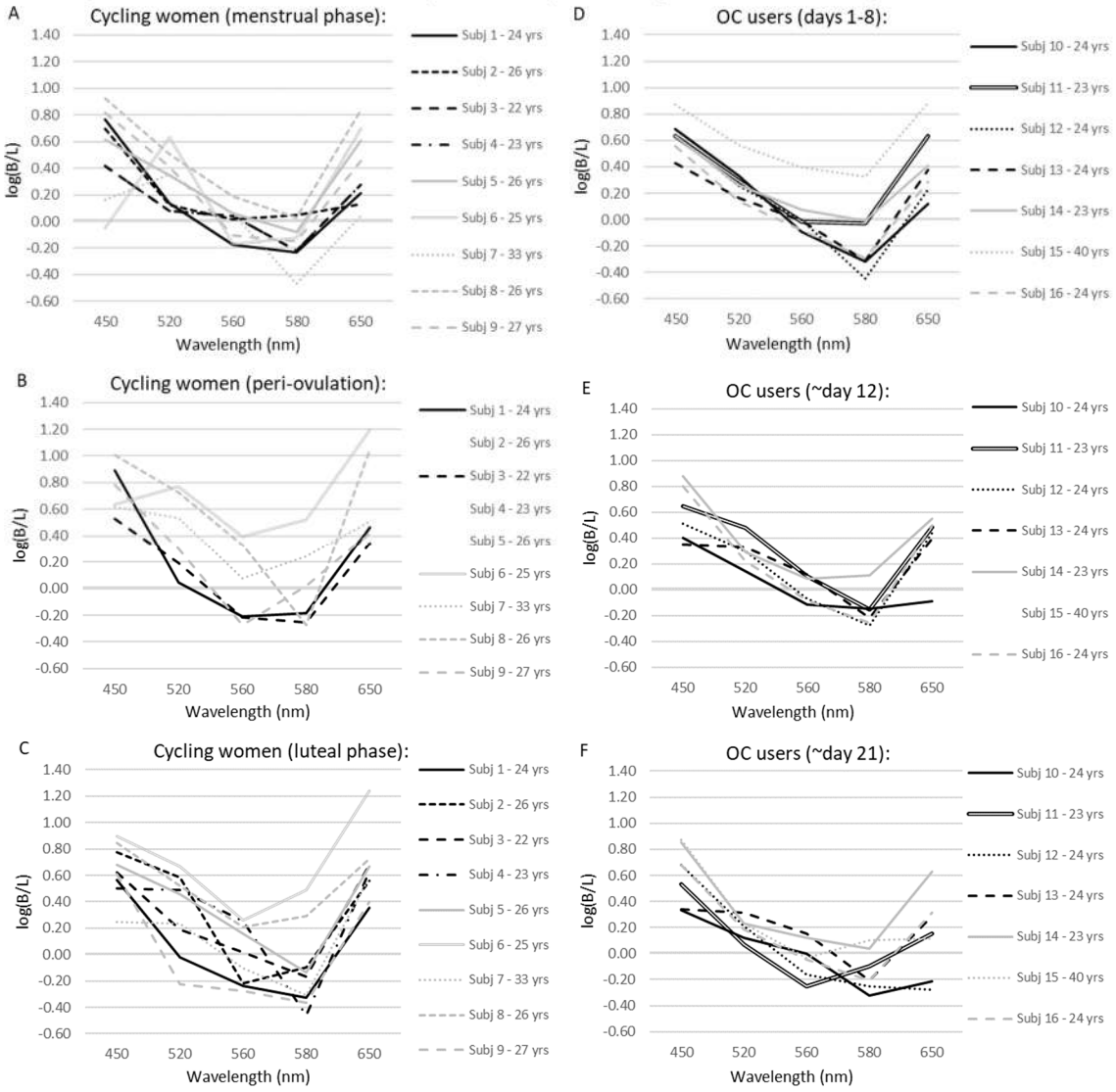

Figure 6. B/L ratios across the menstrual cycle phases for cycling women (A-C) and OC users (D-F). Omitted lines indicate missing data for that session. (Subject numbers are arbitrary for the manuscript.).

4.3. Limitations

Inferences from the present results are first and most limited by the low participation rate in both cycling women (N = 9) and OC user (N = 7) groups. However, there was much expected of participants in terms of cooperation and time. There is growing interest in studies with fewer subjects to switch from inferential (or frequentist) to Bayesian statistical approaches [55]. The current predictions and power analyses were based on previous frequentist assumptions, so it seems unfair (statistically) to do so at this point. However, future investigations could adopt a Bayesian approach and better avoid type II errors possibly encountered in the current study.

The second limitation was in data collection timing. The goal was to collect data for the luteal phase around day 22. Scheduling pressures caused mean luteal data collection to be ~day 20, possibly avoiding predicted mid-luteal estradiol and progesterone peaks. This was a lesson learned and should be avoided in future studies. Third, and most importantly, E2 peaks predicted for the peri-ovulatory phase in cycling women (i.e., E2[peri-ovulatory] < E2[luteal]) were also missed (dee Figure 2A). This result has been seen previously [42] and may be difficult to avoid without additional testing. Inexpensive at-home

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urine ovulation tests could provide an accurate method of verifying peri-ovulation timing and even estrogen surges [56], but coordinating these sessions and the additional testing would have been challenging. The fourth limitation is in the simultaneous reporting of results for cycling women and OC users (as in Table 1 and Figure 3). This has been shown to be inappropriate [57], and Figure 5 clearly shows that modeled B/L ratios fit observed data for cycling women and OC users very differently. Doing so may, however, add legitimacy to the separate treatment of cycling women and OC users in studies of perceived brightness, as the model fit for all participants (R^2 = .59) was less than that for either cycling women (R^2 = .73) or OC users (R^2 = .64). Lastly, salivary hormone levels may well represent circulating bioavailable hormones [58], but commercially available salivary hormone assays underestimate exogenous more so than endogenous hormone levels [39]. This may significantly affect inferences about models including hormones but not luminance and saturation models, which clearly differ by contraceptive use.

5. Conclusions

These results provide clear support for separating cycling women from oral contraceptive users in studies of brightness, particularly when luminance and saturation are predictors—as in the Helmholtz-Kohlrausch effect. In summary, these findings extend the literature on the H-K effect in at least four ways. They establish OC use and menstrual cycle phase as mechanisms for between- and within-subjects variation in brightness. Second, they add E2, P, and their interaction terms to current brightness models for cycling women. Third, the interaction effect of OC use and MC phase on B/L ratios for the red (i.e., 650 nm) stimulus adds to a rich history of long-wavelength (i.e., red) mechanisms. Lastly, hormonal effects on short-wavelength stimuli are different between cycling women and OC users. All these results deserve additional consideration.

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Data Availability Statement: Portions of the data presented in this study may be made available on request from the corresponding author. The data are not publicly available due to health privacy restrictions.

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Conflicts of Interest: The author has reported portions of these data in continuing education lectures and in abstract form as meeting scientific reports but declare no further potential conflict of interest in authorship or reporting.

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