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Original Article

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Exploratory study of the effects of sex and hormonal contraceptives on alertness, fatigue, and sleepiness of police officers on rotating shifts

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Abstract

Study Objectives: This exploratory study assessed the impact of sex and hormonal contraceptives (HC) use on the homeostatic and diurnal variation of alertness, fatigue, sleepiness, psychomotor performance, and sleep behavior in police officers working rotating shifts.

Methods: A total of 56 men and 20 women (6 using, 11 not using, and 3 with unknown use of HC) participated in an observational study throughout a month-long work cycle. Participants wore an actigraph, filled out a sleep and work log, answered questionnaires (Samn-Perelli, KSS, Visual Analogue Scales), and completed 5-min Psychomotor Vigilance Tasks (PVT) according to an ecological momentary assessment approach. Linear mixed-effects models were used to analyze the effects of group (men, women, and HC use), time awake, and time of day on the dependent variables.

Results: Self-reported parameters and performance significantly varied with time awake and time of day. Women were more fatigued and sleepier than men, when considering both time awake and time of day. Compared to men, women using HC were more fatigued, less alert, and sleepier. Women had less attention lapses than men after 7 and 17 h awake, although no main effect of HC was detected.

Conclusions: Women tended to rate themselves as more fatigued than men, especially when using HC. Surprisingly, psychomotor performances of women were sometimes better than those of men. This exploratory study indicates that sex and HC are important factors to consider in occupational medicine.

Key words: shift work; women's health; circadian rhythms; sleep/wake physiology; actigraphy; neurobehavioral performance; sleepiness

Statement of Significance

Differences in sleep, alertness, and circadian parameters have been reported between men and women. However, field studies that compare men and women shift workers are scarce. The results of this study expand our knowledge of the sex differences in sleep and circadian physiology and demonstrate an important effect of hormonal contraceptives on women's self-reported fatigue, sleepiness, and alertness when working shifts.

Introduction

In numerous industries, the need to offer services outside of the conventional weekdays forces individuals to work on shifts that are atypical both in terms of timing and duration. This situation is common in industrialized countries and affects about 10–30% of the workforce [1, 2]. A similar proportion of individuals report working nights at least once a month [3]. Regularly working nights or rotating shifts was reported by as much as 12–13% of North American workers [4, 5]. Importantly, roughly half of the exposed workers in North America and Europe are women [3, 6, 7]. This is of clinical interest since nationwide surveys found the risk of work injuries attributed to shift working to be significantly higher among women [8, 9], suggesting they might be more

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susceptible than men to sleep-wake disturbances when working atypical schedules. Recent evidence also indicates that the risk of negative health problems associated with shift work can be affected by sex and gender [10].

Sleep restriction, extended wake periods, and circadian misalignment are frequent in schedules involving night shifts [11, 12]. The few existing field studies of shift workers comparing men and women revealed women generally report more sleep problems, higher levels of fatigue and sleepiness, more frequent drowsiness at work, higher rates of disability, and more self-reported health complaints when working shifts [10, 13–16], although other studies reported the opposite or no effect [13, 17, 18]. This is not surprising as there is mounting evidence supporting sex differences in sleep and circadian physiology [19, 20].

Considering the prevalence of shift work, its adverse health consequences [10, 21–23], and the sex differences in sleep and circadian physiology [19, 20], it is pressing to improve our scientific knowledge of the sex and gendered impact of atypical work schedules. This is in line with a 2019 Consensus Paper by the Working Time Society which identified sex and gender as important factors modulating tolerance to shift work and called for more research on this issue [13]. Still today, the mechanisms by which sex, gender, and gonadal hormones contribute to the variation of sleep, sleepiness, alertness, and performance with time awake and time of day remains understudied. In addition to sex differences in sleep and circadian physiology [24–27], the variation of reproductive hormones in women across the menstrual cycle [28–33], with menopause [34], and with the use of hormonal contraceptives (HC) [31], can affect alertness and performance. To what extent and by which mechanisms gonadal or gonadotropic hormones modulate the circadian variation of sleep and alertness still remains unclear [35].

Considering that, in Canada only, around 30% of women of reproductive age use HC [36], it is surprising so little is known about their effects on circadian rhythms, the circadian variation of sleep, alertness and performance, or on their impact on shift workers. The aim of the present exploratory study is to assess the impact of sex and HC use on the homeostatic and diurnal variation of self-reported measures of alertness, psychomotor performance, and sleep of patrol police officers working rotating shifts.

Methods

Participants

This is a large field study designed to address several hypotheses on sleep and circadian rhythms of rotating shift workers, such that our group has previously published about the same study population [37, 38]. Police officers were recruited in the province of Quebec, Canada (see flowchart—Supplementary Figure S1). After an advertisement campaign, a total of 231 potential participants contacted the research team. Interested participants answered a screening questionnaire, including questions about past and present medical conditions. To be eligible, police officers had to be on patrol, aged between 20 and 67 years, and be working full-time on rotating shifts. Exclusion criteria included having substantial commitments outside work (e.g. part-time work, military duties, classes, and examinations affecting rest days for ≥10 hr/week), reporting sleep disorders not related to shift working, or any medical complaint, or use of medications that could disturb their sleep or waking. Based on these criteria, 81 police officers were included in the study. From those, five were later excluded (two withdrew consent, two reported medical conditions and one had technical problems during the study). Women provided information regarding their means of contraception and menstrual cycles. Based on this information and clarification when needed, women were classified into two groups according to whether they used (HC) or not (non-HC) hormonal contraceptives. Written informed consent was obtained from all participants.

Study design

This was an observational field study that used an ecological momentary assessment approach [39] in which data were collected daily throughout a complete work cycle (35 or 28 days). The standard 35-day work schedule consisted of morning (starting at 0700 hr), evening (starting at 1500 hr), and night (starting at 1900 hr or 2200 hr) shifts of 9-hr or 12-hr duration, alternating with rest days. The standard 28-day roster consisted exclusively of 12-hr shifts (from 0700 hr to 1900 hr or 1900 hr to 0700 hr), alternating with rest days. Participants were provided with a portable device (Google Nexus 5, LG Electronics, Seoul, South Korea) to fill out daily questionnaires and tests (described below) several times each day. They were also asked to wear an actimetry sensor (Actiwatch Spectrum®, Respironics, Philips, OR) on the non-dominant wrist that collected activity data in 15-s epochs during the entire study, except during baths, showers, or contact sports. Participants were asked to refrain from using sleep drugs or any other medications during the study, or, if needed, to report their consumption to the research team. They were also asked to limit coffee or energy drinks to 3 cups/day and to report the number of energy drinks, alcohol, and cigarettes for each waking period. No rules were imposed regarding their sleep-wake behavior. Throughout the study, participants were contacted by the research team on a weekly basis and 24-hr on-call assistance was provided. The protocol was approved by the Douglas Mental Health University Institute Research Ethics Board and was within the ethical standards of the Declaration of Helsinki.

Measures and variables of interest

Before the study, police officers completed demographic and sleep questionnaires, regarding namely their height and weight, the presence of children at home and their age, the Epworth Sleepiness Scale [40], the Insomnia Severity Index [41], the Horne and Ostberg Morningness–Eveningness Questionnaire (HO chronotype) [42], and the Munich ChronoType Questionnaire (MCTQ) [43]. They also provided the research team with their work schedule to plan the upcoming experiment. The actual hours worked were verified with the participants.

Sleep and time awake.

Actigraphy markers, time-stamped questionnaires, self-reported bedtimes and rise times, activity levels, and light exposure were used in this hierarchical order to determine bed and rise times, and concordance within 15 min between at least two inputs was necessary. If there was no concordance between any of these inputs within 15 min, the process was repeated by using an interval of 30 min. If there was still no concordance, the inputs were considered unreliable and the bedtime or rise time was set manually using activity counts. Sleep was scored using a published sleep detection algorithm [44, 45]. Main sleep episodes, naps, and time awake were then determined, as detailed in a previous publication [37]. In summary, a main sleep episode was defined as the longest sleep episode in a calendar day, and shorter sleep episodes were considered naps. A wake period was defined as the time interval between the main sleep offset and the next main sleep onset. When there were more than 4 hr of missing actigraphy data during a wake period, data collected during that waking period were excluded (out of a total of 3053 sleep periods, 24 (0.8%) were removed because of this criterion). Furthermore, data collected during the 24-hr period of the eastern standard daylight-saving time transitions were excluded (out of 1464 shifts, 7 (0.5%) were associated with a time transition and were therefore excluded). Time awake, that is, time interval between a time-stamped measurement and the prior main sleep offset, was adjusted for naps by removing the sleep duration of all naps occurring between the two-time points. For example, if a measure was taken at 2000 hr with a prior main sleep offset at 0800 hr and a 2-hr nap between these two time points, the time awake for this measure would be 10 hr. In this manuscript, time awake thus refers to the time awake adjusted for nap durations.

Work shifts.

As the schedule worked might differ from the planned schedule, we implemented coherent criteria to categorize shift types as either morning, evening, night, or other shifts, as described previously [37]. If no work occurred during a wake period, it was classified as a rest day. If the reported shifts' length varied between 4.5 and 13.5 hr in duration, they were classified as either morning (start between 0500 hr and 0900 hr), evening (end between 2100 and 0200 hr), or night (start before 0100 hr and end after 0500 hr) shifts. Shifts that did not fall within these durations or start/end time criteria were classified as "other" types (14.5%). All participants had rest days and worked the three types of shifts, except: four participants assigned to a 28-day work roster who did not work any shift that met the criteria of an "evening" shift; one man who did not work any shift in the "morning" category; and two participants (one man, one woman) who had no shifts in the "night" category.

Questionnaires and tests.

During workdays, participants were requested to complete questionnaires at the start, middle and end of their shifts, and at bedtime and rise time, that is, before and after every sleep episode, respectively, including naps. The rise time questionnaires asked for specific information about the prior sleep period, including bedtime, rise time, and estimated sleep quality and duration. During rest days, participants completed questionnaires at rise time and bedtime (n = 26), or at rise time, bedtime, and around 2 hr after rising time, and 2 hr before bedtime (n = 50). These 50 participants were also asked to complete questionnaires when they had a main meal (breakfast, lunch, and dinner) during work and rest days. Self-assessed fatigue (Samn-Perelli 7-point Likert scale, from 1 = "fully alert" to 7 = "completely exhausted") [46], sleepiness (Karolinska Sleepiness Scale, KSS, 9-point Likert scale, from 1 = "extremely alert" to 9 = "very sleepy") [47] and alertness (visual analog scale, VAS, from 0 = "low" to 100 = "high"), were documented at each questionnaire. A 5-min Psychomotor Vigilance Task (PVT) was done at the beginning and end of shifts by all participants. Several participants (n = 50) also completed PVTs during rest days, around 2 hr after rise time and 2 hr before bedtime. The mean response speed (1/reaction time), the mean 10% slowest response speed, and the number of attention lapses (reaction times > 500 ms) were used for further analyses due to their superior conceptual and statistical properties, when compared to other PVT components [48]. Workload was evaluated with the Raw NASA Task Load Index (NASA-TLX) without the weighting scheme [49] at the end of each shift. All measures were time-stamped and participants answered directly on the portable digital device.

Statistical analysis

For the analyses described below, participants were grouped according to sex or hormonal contraceptives use. Thus, variables were either compared between two groups (i.e. 56 men vs. 20 women, n = 76), or between three groups (i.e. 56 men, six HC women, and 11 non-HC women; the three women with uncertain use of hormonal contraceptives were excluded from these analyses, n = 73). All statistical analyses and data visualization were performed with R (R Development Core Team) [50]. Unless otherwise specified, values are reported as mean ± SEM and p-values < 0.05 were considered significant.

Work characteristics.

For the workload evaluation for each participant, the scale scores for each dimension (mental, physical and temporal demands, frustration, effort, and performance) of the NASA-TLX were each analyzed, and then summed, to create an estimate of the overall workload [49]. The results were then averaged per study group.

Sleep-wake behavior.

Total sleep time and sleep distribution across the 24-hr period were calculated from sleep scores derived from 15-s epochs actigraphy data collected during the entire work cycle for each participant. To assess the distribution of sleep across the 24-hr day, the proportion of actigraphically documented sleep, expressed as a percentage of the time spent asleep across the various days, was calculated for each 15-s epoch per participant. Data were then averaged into hourly bins, per participant, then per study group. The area under the curve was calculated to assess the average sleep duration per 24-hr day, per participant, then averaged per study group. A linear mixed-effect model was used to assess the main effects of group, time of day (1-hr bin), and their interaction on sleep quantity across the 24-hr day. Participant ID was included as a random effect and age (continuous), season (categorical: winter, spring, summer, and fall), the children's age group (categorical: no child, at least one child <3 years old, children ≥3 years old), and the children's age group × time of day interaction were added to the model as covariates. These covariates were included based on prior experience with this dataset [37] and because having children influenced sleep propensity at different times of day in preliminary analyses. Post hoc pairwise comparisons with Tukey's adjustments for multiple comparisons [51] were carried out.

Descriptive analyses.

Demographic data, work parameters and workload, sleep parameters (total sleep time, sleep efficiency per main sleep episode or nap, and the number of naps), and behavior were compared using non-parametric Mann–Whitney test for differences between sexes (two groups: men versus women) and using non-parametric Kruskal–Wallis test for differences between the three groups (men, HC women, and non-HC women). The Dunn test (Dunn's Kruskal–Wallis Multiple Comparisons with Benjamini-Hochberg adjustment) was used for post hoc analyses. The number of children (expressed in percentage of the group) was compared between groups using a Yates' χ^2 test.

Table 1. Main characteristics of participants

	Men	Women		*p*-value	Statistics
	(*n* = 56)	(*n* = 20)			
		HC	Non-HC		
		(*n* = 6)	(*n* = 11)		
Age	32.1 ± 0.8	31.9 ± 1.0		0.82	*U* = 580
		28.8 ± 0.7	33.8 ± 1.1	0.049£	χ^2 (2) = 6.02
BMI	25.5 ± 0.3	22.7 ± 0.4		<0.001¥	*U* = 200.5
		22.8 ± 0.7	22.4 ± 0.3	<0.001¥	χ^2 (2) = 17.56
Years of Experience	8.4 ± 0.7	7.1 ± 0.8		0.34	*U* = 470
		5.3 ± 0.6	8.7 ± 1.1	0.19	χ^2 (2) = 3.31
Number of children					
0	41.1%	100%	36.4%	0.26‡	χ^2 (2) = 2.65
1 or 2	51.8%	0%	45.4%	0.052§	
3 or 4	7.1%	0%	18.2%		χ^2 (4) = 9.41
ESS¶	7.1 ± 0.4	8.1 ± 0.6		0.27	*U* = 631
		8.8 ± 1.3	7.9 ± 0.8	0.38	χ^2 (2) = 1.95
ISI¶	8.2 ± 0.6	9.8 ± 1.2		0.23	*U* = 638.5
		11.0 ± 2.5	8.4 ± 1.7	0.58	χ^2 (2) = 1.10
HO chronotype¶	50.9 ± 1.2	51.5 ± 2.2		0.64	*U* = 578.5
		51.7 ± 3.8	50.8 ± 3.3	0.96	χ^2 (2) = 0.09
MSF†	3.3 ± 0.3	3.3 ± 0.3		0.79	*U* = 330.5
		3.8 ± 0.4	2.8 ± 0.4	0.34	χ^2 (2) = 2.14

Values are indicated as means ± SEM, except for the number of children which is expressed as a % of participants. *P*-values are presented for between-group differences.
ESS: Epworth Sleepiness Scale; ISI: Insomnia Severity Index; HC: Hormonal contraceptives; HO: Horne and Ostberg chronotype; MSF: main sleep episode midpoint on rest days measured by MCTQ adapted for shift workers.
¶These specific questionnaires were missing for two men.
†This evaluation was only available for 42 men and 13 women (6 from the HC and 7 from the non-HC groups).
£HC women's age < non-HC women's age: Dunn's Kruskal–Wallis Multiple Comparisons with Benjamini-Hochberg adjustment, Z = 2.41, 95% CI [−8.45, −1.55], *p* = 0.048.
¥Men's BMI > both HC and non-HC women's BMI: Dunn's Kruskal–Wallis Multiple Comparisons with Benjamini-Hochberg adjustment, HC: Z = 2.66, 95% CI [1.00, 4.71], *p* = 0.011; non-HC: Z = 3.55, 95% CI [1.70, 4.80], *p* = 0.0012.
‡*p*-Value for the differences between men and women.
§*p*-Value for the differences between the three groups.

Homeostatic and diurnal variation.

The homeostatic and diurnal variation of the dependent variables (self-reported: fatigue, sleepiness, alertness, and objective: psychomotor performance) were assessed by assigning a time awake since the last main sleep offset, corrected for the duration of naps, as well as a time of day to each observation. Data were then averaged into 2-hr bins of time awake and clock time per participant then per group, except for PVT parameters' time of day, which was averaged into 4-hr bins of clock time. For all dependent variables except attention lapses, linear mixed-effect models (lme4 R package [52]) were used to assess the fixed effects of time awake, time of day, group, as well as the group × time awake, and group × time of day interaction. Attention lapses were analyzed using generalized linear mixed models with a negative binomial distribution (glmmTMB R package [53]), as this count variable showed over-dispersion and a distribution skewed toward zero. Crude analyses were performed with participant ID included as a random effect. Adjusted analyses also included age (continuous), season (categorical: winter, spring, summer, and fall), and the children's age group (categorical: no child, at least one child <3 years old, children ≥3 years old) as covariates. Results from the crude model are presented in the supplementary material only. Post hoc pair-wise comparisons with Tukey's adjustments for multiple comparisons [51] were carried out when necessary. Results of the homeostatic and diurnal variation are presented in two different figures, but they come from a single model for each dependent variable.

Results

Baseline characteristics

A total of 76 police officers (56 men, 20 women) aged 32.0 ± 5.3 years (mean ± SD) completed a field study throughout a work cycle lasting 35 (*n* = 72, 32.1 ± 5.4 years) or 28 (*n* = 4, 29.9 ± 4.1 years, three men and one woman) days. During the study, six women were under hormonal contraceptives (HC women: five took oral contraceptive pills, one had a hormonal intrauterine device), 11 were naturally ovulating (non-HC women: two had a non-hormonal intrauterine device, three did not report the type of contraception used (see flowchart in Supplementary Figure S1). Eight naturally cycling women kept a menstrual cycle log, whereas three did not.

As detailed in Table 1, no significant differences were found between sexes or between the three groups (men, HC women, and non-HC women) regarding baseline sleepiness (Epworth Sleepiness Scale) [40], insomnia severity (Insomnia Severity Index) [41], diurnal preference (HO chronotype) [42], years of experience as a police officer, or the main sleep episode midpoint on rest days [43]. There were group differences in age and BMI. Specifically, HC women were significantly younger than non-HC women and men had significantly higher BMI than the two groups of women.

Work and workload

In total, police officers completed 1457 shifts, including 462 morning, 326 evening, 458 night, and 211 other types of shifts. Neither the shift type proportion, the mean duration of shifts worked, nor the individual and overall workload scores were significantly different between the sexes and between the three groups (detailed results are presented in Supplementary Table S1).

Sleep parameters and behavior

During the entire work cycle (shifts and rest days included), actigraphically documented sleep duration was comparable between sexes and between the three groups based on hormonal contraceptives use in women (see details in Supplementary Table S1). Sleep propensity across the 24-hr day was also similar between sexes (Supplementary Figure S2) and between the three groups based on hormonal contraceptives use in women (Figure 1) when adjusted for having children (among other covariates, for full statistics, see Supplementary Table S2). Having children (at least one child <3 years old or children ≥3 years old) significantly influenced sleep behavior, diminishing the sleep propensity between 0700 and 1000 hr ($p \leq 0.0014$), and increasing it between 2200 and 0300 hr ($p \leq 0.048$, Supplementary Figure S3). As none of the HC women had children, it explains why there was a significant time × group interaction in the crude model (Supplementary Table S2).

Regarding coffee, energy drinks, tobacco, and physical activity, no significant differences were observed (see details in Supplementary Table S1). Men consumed on average more alcohol than women and a significant main effect of group was observed when analyses were based on hormonal contraceptives use in women. However, no significant post hoc differences were observed between the three groups (Dunn's Kruskal–Wallis Multiple Comparisons with Benjamini-Hochberg adjustment, HC vs. non-HC: Z = −0.79, 95% CI [−0.56, 0.22], p = 0.42; HC vs. Men: Z = −2.13, 95% CI [−0.57, 0.05], p = 0.10; Men vs. non-HC: Z = 1.55, 95% CI [−0.06, 038], p = 0.18).

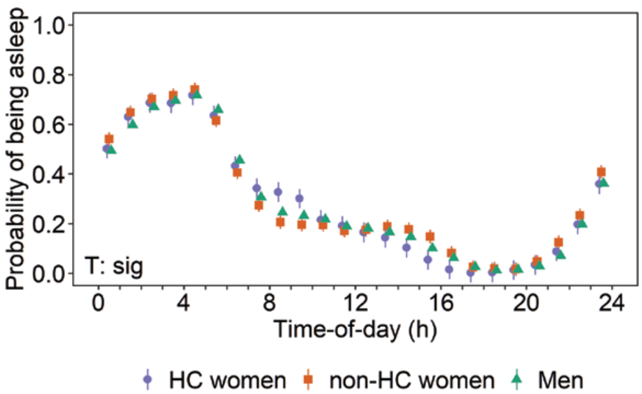

Figure 1. Sleep propensity across the 24-hr day observed among the three groups (men [n = 56], HC women [women using hormonal contraceptives, n = 6], non-HC women [women not using HC, n = 11]) adjusted for age, season and the children's age group. Data points are the estimated marginal mean (± SE) derived from the adjusted linear mixed-effect model of sleep propensity between the groups based on women's hormonal contraceptives use. Annotations indicate significant main effects: T = main effect of time.

Self-reported fatigue, sleepiness, alertness, and psychomotor performance

A total of 37 261 reliable entries were completed by the participants on their portable devices to report their perceived levels of fatigue, sleepiness, and alertness (Samn-Perelli: 12 428; Karolinska Sleepiness Scale: 12 416; Visual analog scale of Alertness: 12 417). From 3710 PVTs completed during the study, 3012 PVTs (81%) were considered reliable and 698 (19%) were excluded because participants indicated being disturbed during the test.

Main effects of time awake and time of day.

A significant main effect of time awake was observed for all dependent variables, whether data were analyzed based on sex or hormonal contraceptives use in women (Figure 2 and Supplementary Figure S4). The only exception was the effect of time awake on the mean 10% slowest response speed when analyzed with groups based on hormonal contraceptives use in women. Time awake increased fatigue and sleepiness levels, and reduced alertness and performance. A significant main effect of time of day was observed for all dependent variables, whether data were analyzed based on sex or hormonal contraceptives use in women (Figure 3 and Supplementary Figure S5). Peak fatigue and sleepiness levels were observed at night and early morning whereas peak alertness and PVT performances were observed in the afternoon and evening.

Effects of sex.

Sex had a significant main effect on fatigue and sleepiness, but not on alertness or PVT parameters (for full statistics, see Supplementary Table S3). Between-sexes analyses revealed that women reported themselves as more fatigued and sleepier than men. A significant interaction between time awake and sex was found for attention lapses, although no main effect of group was found. Post hoc pair-wise comparisons with Tukey's adjustment for multiple comparisons revealed that women had less attention lapses than men after 7 and 17 hr awake (Supplementary Figure S4, 7 hr: −1.20 ± 0.45, 95% CI [−2.09, −0.30], p = 0.0086; 17 hr: −0.92 ± 0.43, 95% CI [−1.76, −0.07], p = 0.033). No significant interaction between sex and time of day was observed.

Effects of HC.

Groups based on hormonal contraceptives use had a significant main effect on fatigue, sleepiness, and alertness, but no effect on PVT parameters (for full statistics, see Supplementary Table S4). Post hoc pair-wise comparisons with Tukey's adjustment for multiple comparisons revealed that HC women reported themselves as more fatigued and less alert than men. No statistical differences were observed between men and non-HC women, nor between the two groups of women.

A significant interaction between time awake and groups based on hormonal contraceptives use in women was found for sleepiness and alertness (Figure 2 and Supplementary Table S4). For sleepiness, post hoc pairwise comparisons with Tukey's adjustment for multiple comparisons revealed that non-HC women reported themselves as sleepier than men after 1 hr awake (+0.85 ± 0.30, 95% CI [0.15, 1.55], p = 0.013). HC women reported themselves as sleepier than men after 9 hr (+1.07 ± 0.44, 95% CI [0.04, 2.1], p = 0.040) and 13 hr (+1.29 ± 0.43, 95% CI [0.28, 2.3], p = 0.0078) awake. After 23 hr awake,

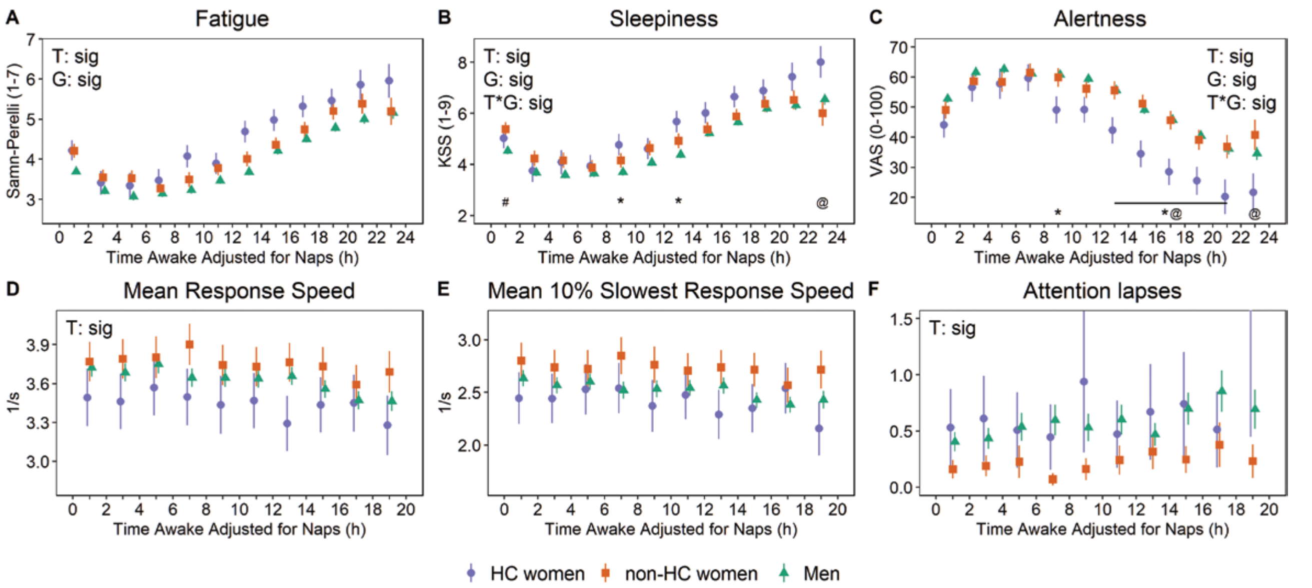

Figure 2. Homeostatic (time awake) variation of self-reported variables (panels A to C) and PVT (panels D to F) between three groups (men [n = 56], HC women [women using HC, *n* = 6], non-HC women [women not using hormonal contraceptives, *n* = 11]) adjusted for age, season and the children's age group. Data are the estimated marginal mean (± SE) derived from the adjusted linear mixed-effect models between the groups based on women's hormonal contraceptives use. Fatigue (Samn-Perelli 7-point Likert scale, from 1 = "fully alert" to 7 = "completely exhausted"), sleepiness (Karolinska Sleepiness Scale, KSS, 9-point Likert scale, from 1 = "extremely alert" to 9 = "very sleepy") and alertness (visual analog scale, VAS, from 0 = "low" to 100 = "high"). Annotations at the top of each panel indicate significant main effects and interaction: *T* = main effect of time, *G* = main effect of group, *T*G* = significant interaction. Results of the mixed-effects models are detailed in Supplementary Table S4. PVT: Psychomotor Vigilance Task. * indicates significant differences between HC women vs. men, and # indicates significant differences between non-HC women vs men and @ indicates significant differences between HC women and non-HC women.

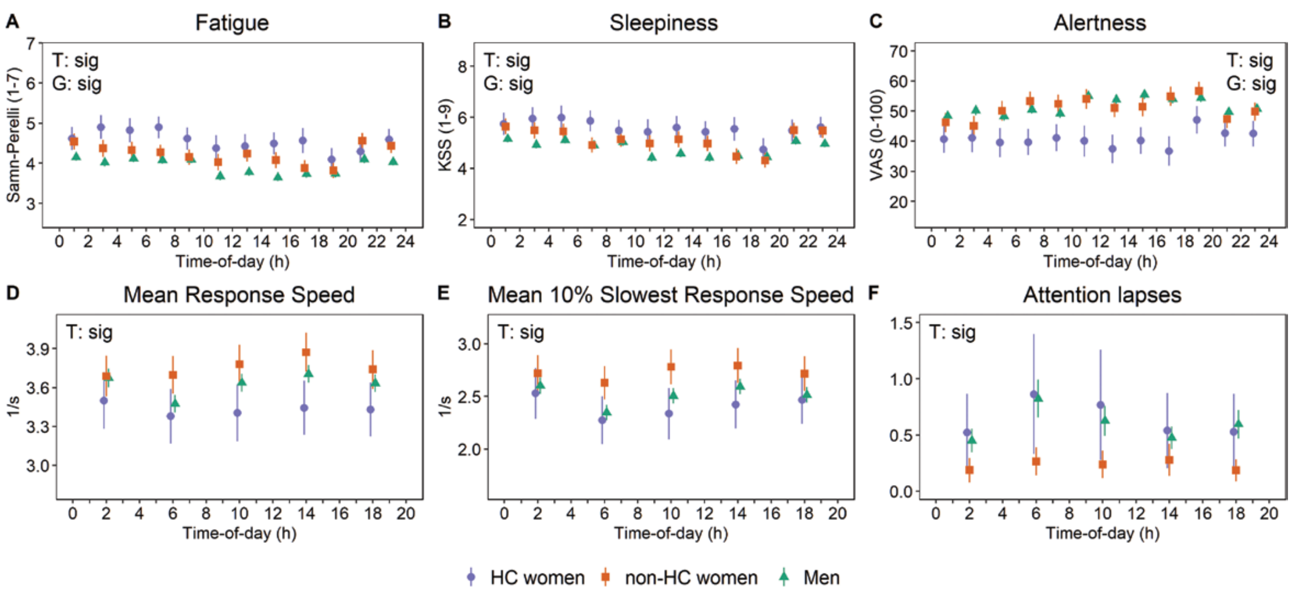

Figure 3. Diurnal (time of day) variation of self-reported measures (panels A to C) and PVT (panels D to F) between groups (men, hormonal contraceptives [HC] women, non-HC women) adjusted for age, season, and the children's age group. Legend as in Figure 2.

HC women reported themselves as sleepier than non-HC women (+2.01 ± 0.78, 95% CI [0.17, 3.85], $p = 0.028$). For alertness, pair-wise comparisons revealed that HC women reported lower alertness levels than men after 9 hr awake (−11.66 ± 4.60, 95% CI [−22.52, −0.80], $p = 0.032$). After 13 to 21 hr awake, HC women reported lower alertness levels than both men (from −13.30 to −17.29, $p < 0.021$) and non-HC women (from −13.25 to −17.16, $p < 0.043$). Finally, after 23 hr awake HC women reported lower alertness levels than non-HC women (−19.13 ± 8.06, 95% CI [−38.04, −0.21], $p = 0.047$). No statistically significant interactions between the time of day and groups based on hormonal contraceptives use in women were found for the six studied parameters.

Discussion

The aim of the present study was to investigate the effects of sex and hormonal contraceptives use in women on self-reported alertness measures and psychomotor performance in police officers working rotating shifts. First, it was observed that time awake and time of day modulate the levels of fatigue, sleepiness, alertness, and psychomotor performance, suggesting that homeostatic and circadian processes are present in real-life settings. In all groups of participants, the lowest levels of self-reported measures and performance were observed with the longest periods of time awake, as well as during the night and early morning hours.

Second, an effect of sex and hormonal contraceptives use in women was observed on these parameters. For self-reported measures, there was a sex difference in the built-up of fatigue levels throughout wake periods, with greater levels of fatigue and sleepiness reported by women. The use of HC in women was affecting self-reported measures as HC women reported themselves as more fatigued, sleepier, and less alert than men, whereas naturally ovulating women did not. The lower alertness levels reported by HC women became more apparent the longer they had been awake, and were significantly higher than that of both men and non-HC women after ~13 to 21 hr of time awake. For objective measures, women presented less attention lapses than men after 7 hr and 17 hr awake. These sex differences appear to be influenced by the lower number of attention lapses in non-HC women, although no significant difference between the three groups was observed. The reason for this interaction is unclear and will require further experimental validation as our sample size is small. As reported previously, self-reported measures and performances do not always change in a coherent manner [54].

The observed effects of sex and hormonal contraceptives use in women on self-reported measures and attention lapses cannot be attributed to differences in sleep behavior. A delayed sleep behavior was observed in HC women as none of them had children, presumably allowing them to go to bed later at night and to sleep later in the morning. However, no group difference in sleep propensity was observed in the fully adjusted model correcting for children's age. Moreover, the amount of sleep cumulated per 24 hr, from main episodes and naps, was comparable between groups, with no evidence of between-group differences in daily sleep pressure. In prior studies, the effects of HC on sleep are inconsistent, with reported longer [55], shorter [56] or similar sleep durations and efficiencies [55, 57–61].

Our results are consistent with those of a prior laboratory study using an ultradian sleep-wake cycle procedure [27], which found that naturally cycling women reported feeling sleepier than men at night during the time of their habitual sleep period, both during the follicular and luteal phases of the menstrual cycle. However, they differ from another study using a forced desynchrony procedure which found that women were less sleepy than men during the biological day only [24]. Of note, in this last study, 9 out of 18 women were on oral contraceptives and the menstrual phase was not controlled for, which could have contributed to the different results between studies.

Prior laboratory studies looking at sex differences in objective performances, using constant routine or forced desynchrony protocols, found lower nocturnal cognitive performances in women compared to men [24, 32, 62]. Unlike those findings, in the present study, women presented less attentional failures after a few durations of time awake, whereas no group difference or interaction was observed for reaction speed. The mismatch between self-reported and objective measures in our study might also reflect a sex (i.e. biological characteristics, hormones) or a gender (i.e. socially constructed role, expression of identity) bias in self-assessment, similar to that reported in investigations on peer and self-assessment [63, 64]. However, this would have to be tested experimentally and we are not aware of any such field study. Our study is exploratory and these results should be confirmed by larger studies, especially considering the variability observed and the small number of HC women. It also remains difficult to compare data collected in the laboratory to those collected in the field as the experimental settings are quite different.

Few studies have looked at the effect of HC on women's sleep, alertness, and performance. Consistent with our results on self-reported measures, it was found in the general population that women taking HC reported more sleepiness and more insomnia symptoms than naturally cycling women [56]. The effect of HC on performances is more controversial with some studies showing a task-dependent effect of oral contraceptives when women were sleep deprived for 24 hr [31], and another study showing similar reaction times in oral contraceptive users and women in the early phase of the menstrual cycle [34]. Unfortunately, in these studies, the authors did not include men, limiting the possible comparisons with our study. The absence of significant differences in objective measures between HC and non-HC women in our study could be explained by our small sample size, which is consistent with a trend for a group difference in PVT lapses. Nevertheless, self-reported alertness levels and sleepiness are important symptoms that impair shift workers' quality of life and should be considered. There are mounting evidences that sex hormones can influence sleep, wakefulness, and their circadian control (for a review [65]), but the precise mechanisms by which this is achieved is unknown. The influence of both endogenous and exogenous reproductive hormones extends to diverse physiological parameters (e.g. systolic blood pressure, heart rate, transepidermal water loss, salivary cortisol, skin amino acids [66]; physical exercise capacity [67]; or spontaneous blink rates [68]), including effects of HC on brain function and neurochemistry [69]. These effects might indirectly impact workers' perceived levels of alertness and fatigue.

Some limitations need to be considered when interpreting the results of our study. We did not take into account menstrual phase in non-HC women, although participants were studied throughout an entire 28–35 day work cycle, so presumably during all phases of their menstrual cycle. Determination of menstrual phase remains a challenge for studies of shift workers as menstrual cycle disturbances are frequent [70] with a reported incidence of 11–19% [71, 72] and prevalence of over 30% [73]. Although we did not perform pregnancy tests, it is highly improbable that participants from the non-HC group became pregnant during the study, as all the eight women who kept menstrual cycle logs continued to menstruate and two used a non-hormonal intrauterine device. The type of hormonal contraceptives in HC women was not determined and could increase variability in this group. HC women were also younger than non-HC women, which could have affected the dependent variables. Nevertheless, our analyses were adjusted for the participant's age, preventing this covariate's interference. The small sample size of our study limits the statistical power to detect differences between the two groups of women such that our results will require further empirical confirmation. This is especially important for the effect of HC as this group is small as well as for the validation of objective performance measures. Participants were either studied on a 35- (n = 72) or 28-day (n = 4) schedule, which could have increased the data variability. However, restricting analyses to participants with a 35-day schedule led to similar results. Another limitation is that police officers were not screened for sleep disorders, although they were excluded if they were receiving a treatment for them.

Baseline excessive daytime sleepiness levels and insomnia symptoms being comparable between the three groups, it is unlikely that intrinsic sleep disorders (e.g. obstructive sleep apnea, periodic limb movements) explain the differences observed in self-reported alertness measures. Finally, our results come from an exploratory study and additional dedicated studies are needed to confirm these findings.

Our study has several strengths such as its within-participant evaluation of sleep and fatigue measures over a complete month-long work roster in each participant. All objective (actigraphy and PVT) and self-reported measures (fatigue, sleepiness, alertness, and workload) collected from the portable device were time-stamped, which moderates reporting bias. Actigraphy is a valid and reliable tool to measure sleep timing and amount in workers [74, 75]. Importantly, our data set is large with more than 37 000 entries for the three questionnaires and PVT, covering around 1500 shifts plus rest days. The study was carried out in a real-world setting and portrays a non-interventional, non-artificially controlled environment. Although field studies are more prone to uncontrolled environmental biases, they have greater ecological validity. Indeed, results from highly controlled laboratory settings cannot be directly transposed to real work conditions where numerous factors (lighting, mental activity, feeding behavior, and stress) might affect alertness, and performance. To the best of our knowledge, this is the first field study comparing the homeostatic and diurnal variation of sleep and alertness of men and women shift workers, with and without HC use.

In conclusion, sex and HC use influenced self-reported alertness, fatigue, and sleepiness levels when working rotating shifts. Sex also significantly influenced attention lapses. Dividing workers only by sex might not completely reflect factors influenced by hormonal parameters and thus future research on shift workers should ideally consider sex, HC use, menstrual phase, and menopausal status. This line of research is relevant to occupational health clinicians and stakeholders concerned with the health and safety of shift workers and the public. It can generate important scientific evidence to guide personalized medicine and fatigue management approaches, although it remains unclear how the integration of such knowledge into workplace operations can be achieved in full respect of workers' private life and work opportunities.

Supplementary Material

Supplementary material is available at *SLEEP Advances* online.

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Author Contributions

DBB designed and supervised all aspects of the study with the help of PB; PB and FGA collected the data with the help of the laboratory staff; all authors were involved in data curation; PB and GMC performed the statistical analyses specific to this manuscript; DBB and GMC wrote the manuscript with support from PB. All authors reviewed and commented on the manuscript.

Conflict of Interest

Financial disclosure: DBB provides conferences and legal expert advice on sleep-related topics. Nonfinancial disclosure: None.

Preprint Repositories

A previous and less detailed different version of the manuscript is available at SSRN 3633228 (preprints with the Lancet, posted on the 30th of June 2020: https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3633228).

Data Availability Statement

The data underlying this article cannot be shared publicly because participants and their organizations have not agreed that their data be placed in a publicly accessible database. Thus, for ethical and confidentiality reasons, the authors cannot provide public access to these data. Nevertheless, materials, data, and associated protocols will be made available for investigation of scientific integrity if necessary. Readers are free to contact the principal investigator if they wish to initiate discussions regarding research collaborations to build on these published data.

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