Peer Community in Registered Reports: Stage 1 Snapshot

1. Provisional title

Influence of sex steroid hormones on the neuroendocrine effects of evening light exposure in healthy young adults

2. Authors and affiliations

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3. Field and keywords

chronobiology, circadian neuroscience, visual neuroscience, non-visual effects of light, melatonin, sex differences, sex hormones, menstrual cycle

4. Research question(s) and/or theory

RQ1: Do female and male participants differ in the amount of melatonin suppression by evening light?

RQ2: Do individuals with different sex steroid hormone profiles differ in melatonin suppression?

RQ3: Do endogenous sex steroid hormones influence melatonin suppression across the menstrual cycle?

RQ4: Do exogenous sex steroid hormones influence melatonin suppression across the contraceptive pill cycle?

RQ5: Are sex differences in light sensitivity present earlier along the non-visual pathway, measured using photoreceptor-selective pupillometry targeting melanopsin?

5. Hypotheses (where applicable)

Confirmatory CH1a: We hypothesise an effect of sex on melatonin suppression outcomes, with female participants exhibiting greater melatonin suppression by bright light compared to male participants.

Confirmatory CH1b: We hypothesise an effect of sex on melanopsin sensitivity, whereby females exhibit higher melanopsin-mediated pupil responses than males.

Confirmatory CH2: We hypothesise that melatonin suppression differs between naturally cycling individuals (NC group), individuals taking monophasic combined oral contraceptives (MCOC group), and male participants (HM group).

Confirmatory CH3: In the NC group, we hypothesise an effect of endogenous sex steroid hormones estradiol (E2) and progesterone (P4) on melatonin suppression.

Confirmatory CH4: In the MCOC group, we hypothesise an effect of ethinylestradiol (EE) and synthetic progestin (SP) on melatonin suppression.

6. Study design and methods

In this within-subjects study, healthy participants (aged 23-35) will perform four experimental sessions in the evening from 7 hours from habitual bedtime (HBT) to 1 hour after HBT. Melanopsin sensitivity and melatonin suppression by bright light from a head-mounted display (~90 lux melanopic equivalent daylight illuminance) will be measured. Sample size is set to a maximum of n=12 for each group (total n=36) due to resource limitations, with careful simulations to be performed using the Bayes Factor Design Analysis framework. For the NC group, cycle tracking using at-home ovulation tests and menses onset reporting will be used to schedule experimental visits during the mid-follicular, late-follicular, mid-luteal, and peri-menstrual phases, thus capturing four different hormonal levels. For the MCOC group, weekly experimental sessions over four weeks will be scheduled to capture hormonal levels during the pill active (n=3 visits) and inactive (n=1 visit) phases. HM group participants will perform weekly experimental sessions over four weeks to match the experimental visits of the NC and MCOC groups. All participants will undergo an additional session in which melatonin will be measured in dim light (<10 lx) as a control to calculate melatonin suppression.

7. Key analyses that will test the hypotheses and/or answer the research question(s)

All confirmatory hypotheses will be examined using linear mixed-effects models implemented in the R package *lme4*, and the Bayes Factor (BF) will be used to calculate the evidence strength of each hypothesis (conclusive evidence for a given hypothesis: BF>10). For CH1a and CH1b, the fixed effects will be sex and light history. For CH2, the fixed effects of interest will be group (NC/MCOC/HM) and light history. For CH3, the fixed effects will be E2 levels, P4 levels and E2×P4 levels interaction. For CH4, EE levels, SP levels, and EE×SP levels interaction will be used as fixed effects.

8. Conclusions that will be drawn given different results

The results of our study will contribute to the growing evidence on potential sex differences in non-visual effects of light and its directionality. Furthermore, by performing repeated sampling in three groups with different hormonal profiles, we will characterise whether sex steroid hormones contribute to these differences. Lastly, by investigating melanopsin sensitivity in addition to melatonin suppression, we will examine where along the non-visual pathway sex differences in light sensitivity may arise, thereby providing key mechanistic insight.

9. Key references

1. Vidafar et al. (2024), https://doi.org/10.1111/jpi.12936

2. Schmalenberger et al. (2021), https://doi.org/10.1016/j.psyneuen.2020.104895

3. Mong et al. (2011), https://doi.org/10.1523/JNEUROSCI.4175-11.2011