The Role of Estradiol in Modifying Circadian Rhythms, Sleep Regularity, and Risk for Depression During the Pubertal Transition

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Introduction

- During the pubertal transition (mid-puberty):
  - dramatic reproductive hormone fluctuations
  - developmental circadian delay
  - significant changes in sleep/wake patterns
- Starting at puberty, female adolescents are 3x more likely to develop depression and 2x more likely to experience sleep disorders compared with males. The involvement of sex hormones is greater in sleep irregularity.
- Greater sleep irregularity is associated with affective impairment.

Objective

Characterize the pathophysiological impact of estradiol on sleep disturbances, endocrine rhythm dysregulation, and depressive symptoms in peripubertal female adolescents.

Methods

- Female adolescents 11-14 years old
- Within 1-year post-menarche
- Chronotype preference
- Daily E1G via dried urine
- Weekly CES-DC and PROMIS sleep measures
- Daily actigraphy starting day 7
- Daily cortisol and melatonin via dried urine days 9-12

Measures

- Superscience Morningness/Eveningness Scale: scored 10-42, with higher scores indicating morningness preference, measure of chronotype
- E1G: urinary metabolite of estradiol, collected once each morning; sensitivity analysis determined mood sensitivity to E1G change
- Center for Epidemiological Studies Depression Scale for Children (CES-DC): scored 0-60, with higher scores indicating greater depressive symptoms; used max score from weekly ratings
- PROMIS sleep measures: Sleep-Related Impairment and Sleep Disturbance surveys; higher scores indicate greater sleep impairment and disturbance, respectively; used max score from weekly ratings
- Sleep Regularity Index (SRI): scored 0-100, with higher scores indicating more regular sleep; calculated from actigraphy scores
- Cortisol and melatonin AUC: calculated from 4 samples collected just after waking, 30 min after waking, at dinner time, and before bedtime
- Cortisol Awakening Response: calculated from slope between first two time points of the day

Results

- Blunted cortisol and increased melatonin predict greater sleep irregularity, which further predicts depressive symptoms
- Greater sleep irregularity, blunted cortisol, and increased melatonin may contribute to increased depressive symptoms in peripubertal female adolescents

Discussion

- Results provide insight into the impact of COVID-19 on sleep and mood in female adolescents
- Approaches that aim to improve consistency of sleep schedules, such as light therapy, may be a promising treatment target for adolescent depression
- Disruptions in HPA diurnal rhythms may predict who is mood sensitive to changes in estradiol

Acknowledgments

Funding: National Institute of Mental Health K01MH121575; Foundation of Hope for Research and Treatment of Mental Illness, Seed Grant


Participant Characteristics (n=47)

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<thead>
<tr>
<th></th>
<th>Range</th>
<th>Mean (SD)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>11–14</td>
<td>12.9 (1.0)</td>
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<tr>
<td>Chronotype Preference</td>
<td>14–39</td>
<td>27.3 (4.7)</td>
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<tr>
<td>Max Sleep-Related Impairment</td>
<td>37.9–73.2</td>
<td>56.8 (6.8)</td>
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<tr>
<td>Max Sleep Disturbance</td>
<td>45.9–72.6</td>
<td>58.4 (7.0)</td>
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<tr>
<td>SRI*</td>
<td>32.8–70.6</td>
<td>54.6 (11.0)</td>
</tr>
<tr>
<td>Max CES-DC**</td>
<td>4–41</td>
<td>19.5 (10.0)</td>
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*In an adult study, SRI < 60.8 indicated irregular sleep
**CES-DC > 15 indicates clinically significant depressive symptoms
66% White, 13% Black or African-American, 9% Asian, 11% more than one race, 2% other; 11% Hispanic and/or Latina

All participants were enrolled after onset of the COVID-19 pandemic.

Greater sleep irregularity, blunted cortisol, and increased melatonin may contribute to increased depressive symptoms in peripubertal female adolescents.