Do Toxicants Affect Adolescent Sleep?

Findings from the ELEMENT Study

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Why do adolescents need sleep?

- Academic performance
- Mental health
- Motor vehicle accidents
- Risky behavior
- Lower immunity
- Poor diet quality

- Adverse cardiometabolic health

Adiposity in Adolescents: The Interplay of Sleep Duration and Sleep Variability

Bedtimes and Blood Pressure: A Prospective Cohort Study of Mexican Adolescents

The Association Between Sleep Duration and Sleep Timing and Insulin Resistance Among Adolescents in Mexico City

Adolescents: vulnerable population

Insufficient sleep: 60% of US middle schoolers

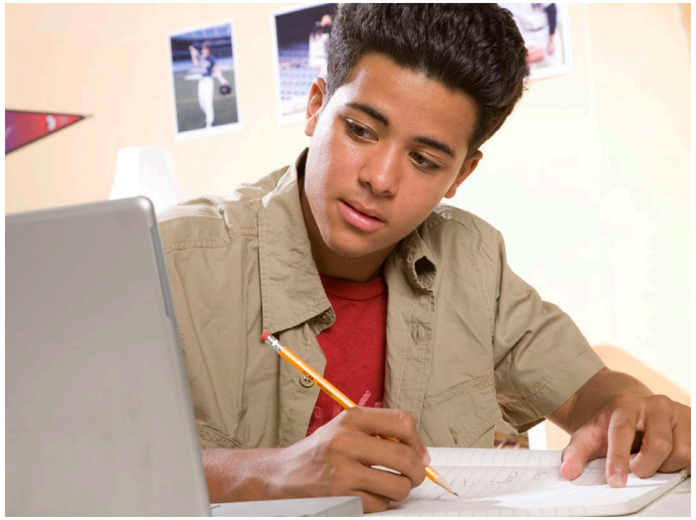
Should be getting 9-12

Insufficient sleep: 70% of US high schoolers

Should be getting 8-10

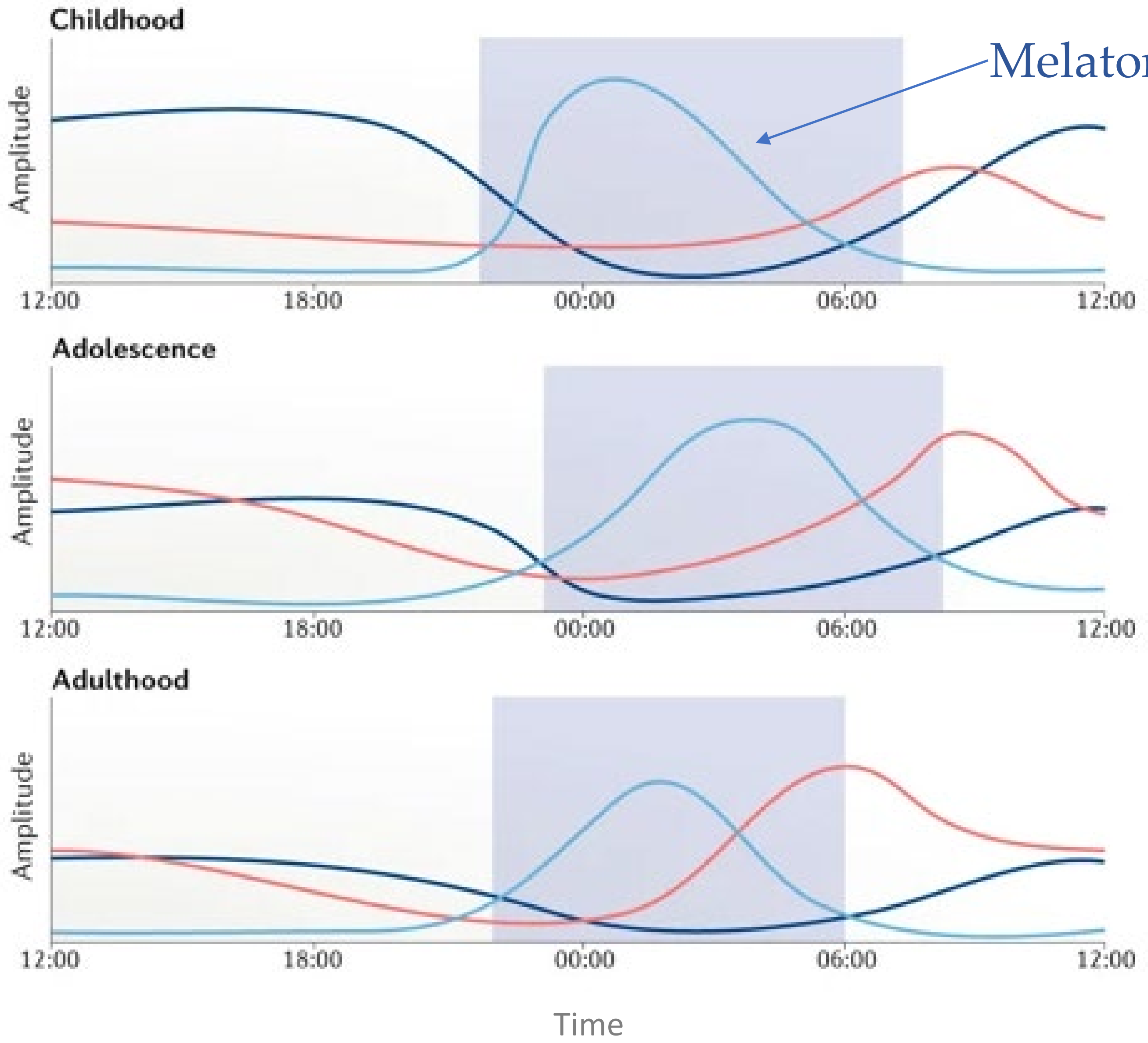
Wheaton AG, Jones SE, Cooper AC, Croft JB. Short Sleep Duration Among Middle School and High School Students — United States, 2015. MMWR Morb Mortal Wkly Rep 2018;67:85–90.

Why won’t they sleep?



Why can’t they sleep?

Natural phase delay



Melatonin

Shifted bedtimes

Logan and McClung. 2019. *Nat Rev Neurosci*;20(1):49-65.

Other things affecting their sleep?

Jansen et al. *Public Health Nutr* **2021**,
DOI: https://doi.org/10.1017/S136898002100313X

Jansen et al. *Nutrients* **2020**, *12*(8),
2305; **https://doi.org/10.3390/nu12082305**

Diet as a source of Pb in Mexico

Could lead affect sleep in adolescents?

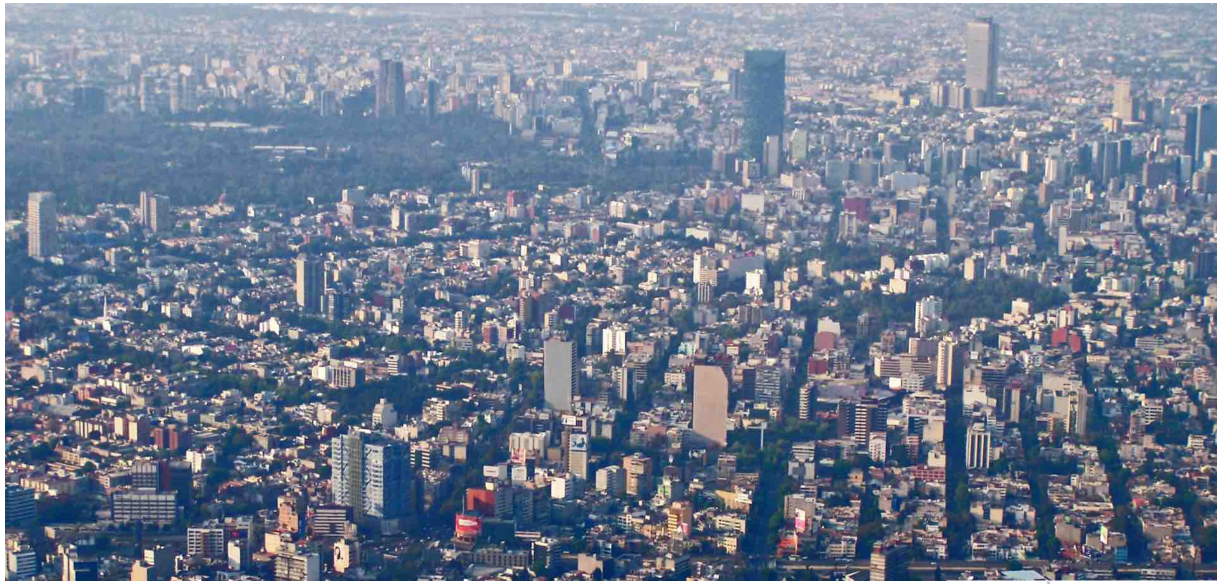
- One study[1] in early childhood with parent-reported sleep

- Links between toxicant exposures and neurodevelopmental outcomes

[1] Liu et al. *Sleep* 2015 Dec 1; 38(12): 1869–1874.

Early Life Exposures to Environmental Toxicants (ELEMENT) Cohort

Birth cohort study



Adolescent visit- 2015 to 2016

550 adolescents, aged 9 to 17 years

ELEMENT

Early Life Exposure in Mexico to Environmental Toxicants Project

Lead assessment

Annual whole blood samples from ages 1-4

Cumulative BLL from ages 1-4 calculated by estimating the area under the curve

Sleep Assessment

GT3X-BT Actigraph

Sleep diary

PDP approach[1] for estimation

N=531 participants

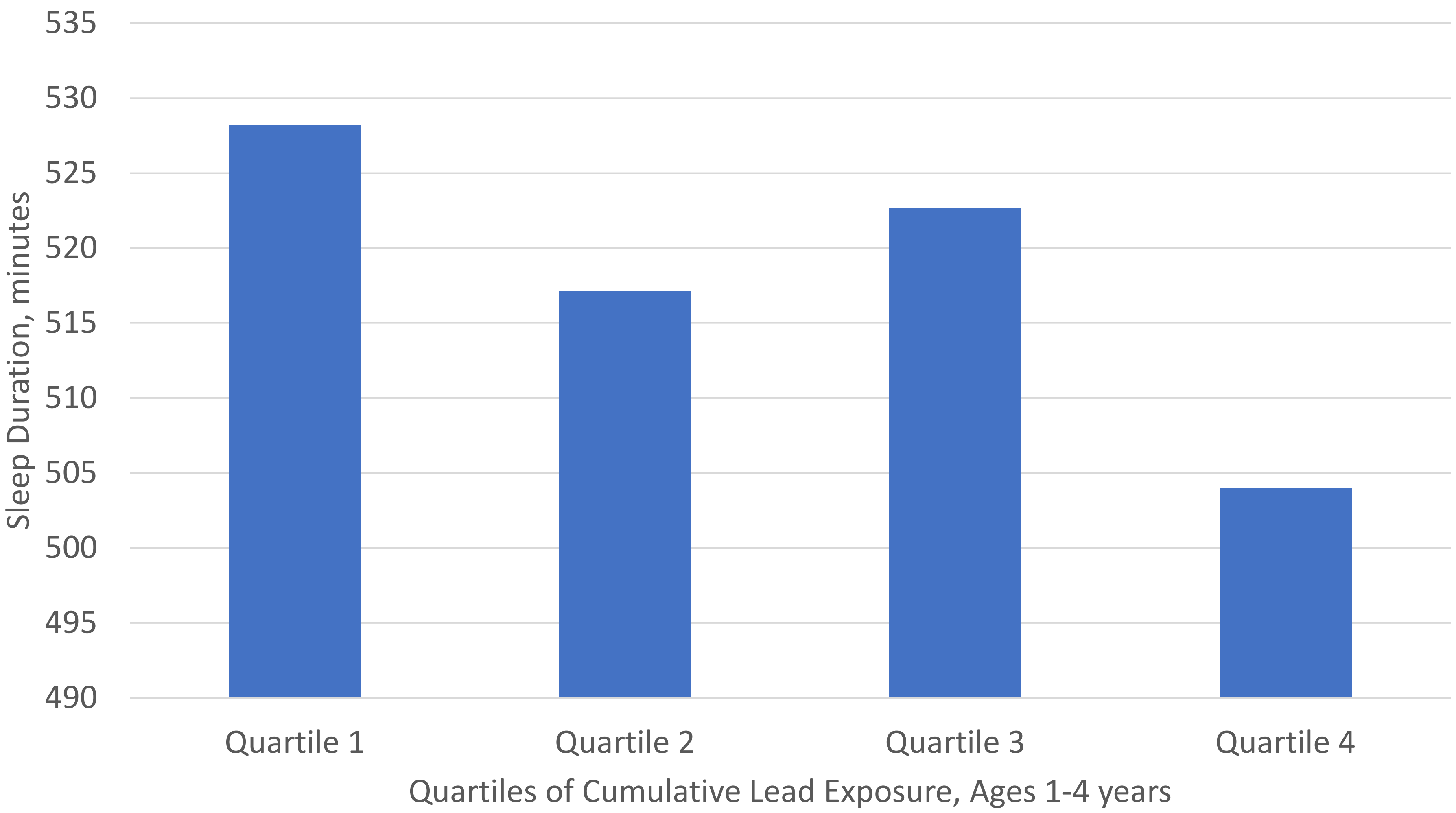
[1]Baek, J et al. *Statistics in Biosciences* 2021

Descriptive Statistics

- Average age: 13.8 years old (SD=1.9)
- 48% male
- 80% in latter stages of puberty
- 38% of sample had BLL>5 ug/dL at any given time point

social worker administering questionnaire

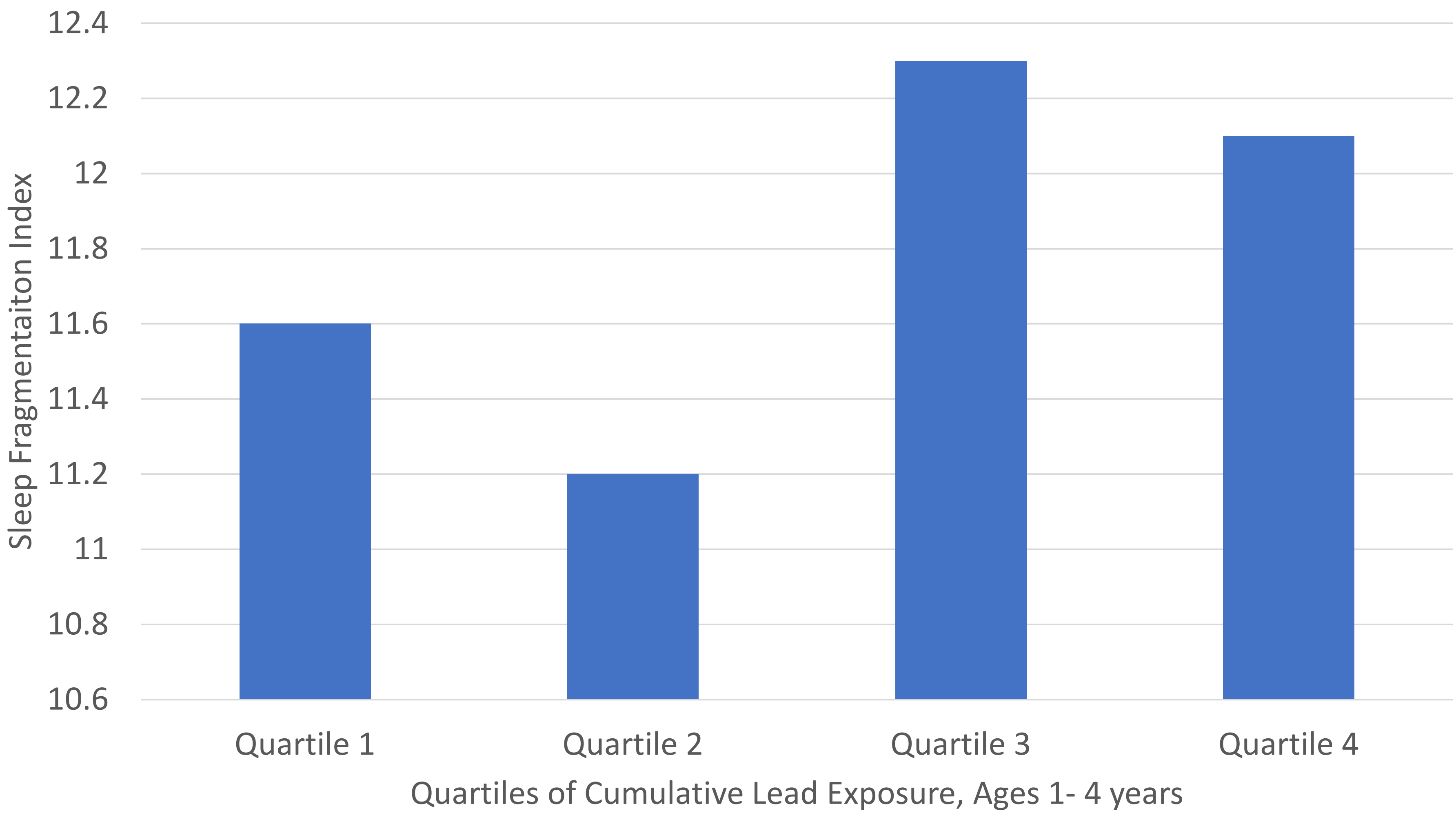
Results



Jansen et al. *J Clin Sleep Med* **2019**,
DOI:https://doi.org/10.5664/jcsm.7972

23-minute difference (adjusted for sex, age, and maternal education)

Results

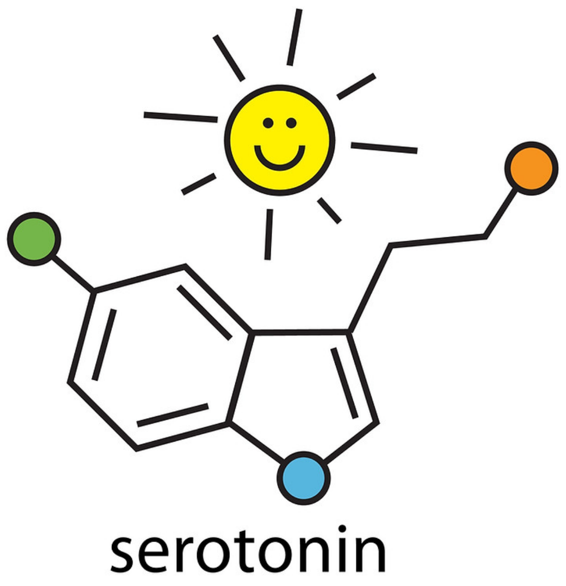


Jansen et al. *J Clin Sleep Med* **2019**,
DOI:https://doi.org/10.5664/jcsm.7972

1.5% difference (adjusted for sex, age, and maternal education)

What did we learn?

- Higher cumulative exposure to lead associated with shorter sleep duration
- Higher cumulative exposure to lead associated with higher sleep fragmentation, but only among younger adolescents
- Potential mechanism through serotonin



Limitations

- Actigraphy does not distinguish asleep vs in-bed
- Not clear how early-childhood exposure to lead persisted over time
- Potential confounding by neighborhood or household-level factors

Other toxicants: pesticides and mercury

Environmental Research 204 (2022) 111977

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Prenatal maternal pesticide exposure in relation to sleep health of offspring during adolescence

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ARTICLE INFO

Keywords:
Chlorpyrifos
Pyrethroids
Pesticides
Early-life exposures
Sleep health

ABSTRACT

Study objectives: The neurobiological processes involved in establishing sleep regulation are vulnerable to environmental exposures as early as seven weeks of gestation. Studies have linked *in utero* pesticide exposure to childhood sleep-disordered breathing. However, the impact of *in utero* pesticide exposure on the sleep health of adolescents remains unexplored.
Materials and methods: Data from 137 mother-adolescent pairs from a Mexico City cohort were analyzed. We used maternal urinary 3-phenoxybenzoic acid (3-PBA, pyrethroid metabolite) and 3, 5, 6-trichloro-2-pyridinol (TCPy, chlorpyrifos metabolite) from trimester three to estimate *in utero* pesticide exposure. Among adolescents, we obtained repeated measures of objectively assessed sleep duration, midpoint, and fragmentation using wrist-actigraphy devices for 7 consecutive days in 2015 and 2017. Unstratified and sex-stratified associations between maternal urinary 3-PBA and TCPy and adolescent sleep measures were examined using generalized linear mixed models (GLMMs). We also examined the interactive effects of maternal pesticide exposure and offspring sex on sleep outcomes.
Results: 3-PBA and TCPy were detected in 44.4% and 93% of urine samples, respectively. Adjusted findings demonstrated that higher exposure to maternal TCPy was associated with longer sleep duration and later sleep timing. Findings from interaction tests between maternal pesticide exposure and offspring sex were not statistically significant, although adjusted sex-stratified findings showed that the association between TCPy with duration and midpoint was evident only among female offspring. To illustrate, those in the highest tertile of exposure had a 59 minute (95% CI: 12.2, 104.8) (p, trend = 0.004) longer sleep duration and a 0.6 hour (95% CI: 0.01, 1.3) (p, trend = 0.01) later sleep midpoint. We found no significant associations between 3-PBA and sleep outcomes.

Environmental Research 191 (2020) 110216

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Mercury exposure in relation to sleep duration, timing, and fragmentation among adolescents in Mexico City

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ARTICLE INFO

Keywords:
Mercury
Neurotoxicant
Sleep
Circadian
Adolescence

ABSTRACT

Introduction: Mercury intoxication is known to be associated with adverse symptoms of fatigue and sleep disturbances, but whether low-level mercury exposure could affect sleep remains unclear. In particular, children may be especially vulnerable to both mercury exposures and to poor sleep. We sought to examine associations between mercury levels and sleep disturbances in Mexican youth.
Methods: The study sample comprised 372 youth from the Early Life Exposures to Environmental Toxicants (ELEMENT) cohort, a birth cohort from Mexico City. Sleep (via 7-day actigraphy) and concurrent urine mercury were assessed during a 2015 follow-up visit. Mercury was also assessed in mid-childhood hair, blood, and urine during an earlier study visit, and was considered a secondary analysis. We used linear regression and varying coefficient models to examine non-linear associations between Hg exposure biomarkers and sleep duration, timing, and fragmentation. Unstratified and sex-stratified analyses were adjusted for age and maternal education.
Results: During the 2015 visit, participants were 13.3 ± 1.9 years, and 48% were male. There was not a cross-sectional association between urine Hg and sleep characteristics. In secondary analysis using earlier biomarkers of Hg, lower and higher blood Hg exposure was associated with longer sleep duration among girls only. In both boys and girls, Hg biomarker levels in 2008 were associated with later adolescent sleep midpoint (for Hg urine in girls, and for blood Hg in boys). For girls, each unit log Hg was associated with 0.2 h later midpoint (95% CI 0 to 0.4), and for boys each unit log Hg was associated with a 0.4 h later sleep midpoint (95% CI 0.1 to 0.8).
Conclusions: There were mostly null associations between Hg exposure and sleep characteristics among Mexican children. Yet, in both boys and girls, higher Hg exposure in mid-childhood (measured in urine and blood, respectively) was related to later sleep timing in adolescence.

Future directions

- Epigenetic mechanisms
- Consider interactions between diet and toxicants
- Ultimately, does reducing exposures improve sleep?

Acknowledgments

- Collaborators and Mentors: Drs. Karen Peterson, Mara Tellez-Rojo, Dana Dolinoy, Jaclyn Goodrich, Helen Burgess, Louise O'Brien, Alejandra Cantoral, Galit Dunietz, Peter Song, Jonggyu Baek

- Students: Aleena Dababneh, Margaret Banker, Astrid Zamora

- NIH support
  - T32 HL11095
  - K01 HL151673
  - P01 ES02284401
  - P30 ES017885

- Study teams and participants in Mexico

ELEMENT
Early Life Exposure in Mexico to Environmental Toxicants Project