SLEEP AND PHYSICAL ACTIVITY PATTERNS IN AUTISM

MAJA BUĆAN, PhD
Perelman School of Medicine,
University of Pennsylvania
Financial disclosures

None
Autism Spectrum Disorder
We study ASD-linked traits and conditions:

- To gain mechanistic understanding of underlying impairments and the relationship between core features and common comorbidities;
- To find ways to alleviate or reduce common comorbidities and improve lives of individuals with ASD;
- To identify target symptom domains that may be responsive to pharmacological treatment.
Why sleep?

- Sleep problems are common in ASD;
- Sleep often represent an early sign of ASD and plays an essential role in brain development;
- The synaptic dysregulation may lead to ASD and sleep disturbances;
- Sleep/activity traits are amenable to continuous data collection in humans and model organisms.
Sleep problems and sleep diagnoses reported by caregivers in SPARK

Based on data from Fombonne....SPARK Consortium, *J Autism Dev Disord*, 3679-3698, 2020
The two-process model of sleep

Synapse development and function

ASD  ?  Sleep:wake rhythms
Lab and ambulatory PSG set-up at home require a prolonged systematic desensitization period.

Polysomnography

Multiple sensors:

EEG - brain waves
EOG - eye movement
EMG - muscle tone
ECG - heart rhythms
Airflow sensors

“Lab and ambulatory PSG set-up at home require a prolonged systematic desensitization period”.

Primeau…..O’Hara, Journal of Clinical Sleep Medicine 12, 2016
SLEEP IN CHILDREN WITH AUTISM SPECTRUM DISORDERS

Sleep Behaviors and Sleep Quality in Children with Autism Spectrum Disorders

Margaret C. Souders, PhD, CRNP; Thorton B. A. Mason, MD, PhD, MSCE; Otto Valladares, MS; Maja Bucan, PhD; Susan E. Levy, MD; David S. Mandell, ScD; Terri E. Weaver, PhD, RN, FAAN; Jennifer Pinto-Martin, PhD, MPH.
Actimetry devices

Philips Respironics Actiwatch
GENEAActiv
Axivity AX3
FitBit
OURA
Apple Watch
Actigraph – double plotted record for 3-week long recording

Relative amplitude

RA = (M10-L5)/(M10+L5)
Actimetry-derived sleep and physical activity traits

Day 3: Sunday 1 27 Aug 2023

Angle of sensor's z-axis relative to horizontal plane:

Arm movement:

Sleep onset

Movement

Sleep

Temperature

Light

Night: 2

Night: 3
Sleep and activity scoring algorithms

**GGIR** (for GENEActiv and GENEA data In R)
van Hees et al., *Scientific Reports*, 2018

**ChronoSapiens A12 (©2020 Chronsulting UG)**
Winnebeck…Ronneberg, *Current Biology*, 2018

**Accelerometer** – for classification of physical activity traits
Doherty et al., *Nat Commun*, 2018
Twin-based heritability of actimetry traits

Philip R. Gehrman¹  |  Arpita Ghorai²  |  Matthew Goodman²
Richard McCluskey⁵  |  Holly Barilla¹  |  Laura Almasy²,³  |  Till Roenneberg⁴
Maja Bucan¹,²
Ongoing ASPE and SPARK study of sleep and activity in ASD

ASPE

140 ASD subjects
229 family members

Simons Powering Autism Research (SPARK)

200/700 ASD probands

3 weeks of actimetry data

Social Responsiveness Scale (SRS)
Broad Autism Phenotype Questionnaire (BAPQ)
Behavioral Rating Inventory of Executive Function (BRIEF)

250 measures!!!

ESS, PROMISE (Sleep)
Glasgow Sensitivity Questionnaire
Relationship between the core and ASD-linked traits
SPARK PARTICIPANTS - GSQ

Glasgow Sensory Questionnaire, v1.2

SPARK participants - GSQ

Glasgow Sensory Questionnaire, v1.2

SPARK participants – PROMIS
Sleep disturbances

PROMIS Disturb Score N = 679, Mean = 79
Examples of activity patterns in individuals with ASD
Activity pattern over a year long period of a child with autism

Modified from: Segawa and Nomura, in Autism: A neurological disorder of early brain development
Tuchman and Rapin, 2006
Rare, predicted deleterious variants in sleep and clock genes in SPARK ASD subjects

CADD > 20
or
REVEL ≥ 0.5
MAF 0.1%
Our findings to date

• Actimetry can be conducted over prolonged periods, enabling assessment of sleep dynamics and activity on a scale sufficient for genetic investigations;

• ASD probands show lower level of physical activity during the day and a high degree of variability across both sleep and activity traits;

• Integration of human genetics findings in ASD families with parallel studies in model organisms will be necessary for our deeper understanding of synaptic imbalance in ASD and associated sleep problems.
Our challenges

Genetic heterogeneity;

A high degree of day-to-day variability in sleep and activity patterns;

Sex differences in sleep and activity patterns;

Significant age differences in sleep and activity pattern:
    a need for longitudinal sleep/activity monitoring;

A need for integration of data from multiple sensors:
    activity, EEG, heart rate, heart rate variability, oxygen saturation etc.
Simons Sleep Project (pilot)
(Dr. Ilan Dinstein, PI)

100 families with one ASD and one non-ASD siblings ages 10-17yo
Recording sleep over 2-3 weeks
LOOKING AHEAD

One day, the sleep and activity patterns collected by a wearable device will be an actionable part of the clinical care of an individual with ASD..........

.....but we need help from computer and data scientists to make sense of the vast amount of data generated by a wide array of wearable devices that sense both our biology and our environment.
ACKNOWLEDGEMENTS:

Thanks to ASPE and SPARK participants and their families!

Jing Zhang
Arpita Ghorai
Dylan van Kampen
Thaise Carneiro
Dana Karson

Ted Brodkin
Holly Dow
Maya Rajan

Laura Almasy
Joe Zhou
Mike Hart
Tom Jongens
Dan Rader

Till Roenneberg
Matt Kayser
Ilan Dinstein

Dan Rader
Maria Fasolino

NIH: R21-MH093415
SFARI-Human Award # 877185

Thanks to our donor for a generous philanthropic gift to ASPE!

Autism Spectrum Program of Excellence