

Sleep Uncovered: Developing Electrophysiologic Sleep Phenotyping (ESP) Biomarkers in Neurodevelopmental Disorders

Exploring Sleep Disturbance in Central Nervous System Disorders: A Workshop

National Academies of Sciences, Engineering & Medicine

November 2nd , 2022



Ashura Williams Buckley, MD, FAAP
Neurology
Child Neurology
Sleep Medicine



National Institute of Mental Health

With thanks...

To the children and families who participate in our research

Sleep Mentors

Ken Sassower
Susumu Sato
Al Rechtschaffen
Alcibiades Rodriguez

Sleep & Neurodevelopmental Service



Patrick Sorenson
Matt Brannan
Josiah Koleosho
Daniel Ephrem
Dieudonne Samuel
Amanda Kuhn
Averie Dickinson
Justine Hayward
Thiane Gaye
Xinyi Hong
Jacob Collen
Omar Khan
Hailie Suarez
Lucy Block
Cheri McNeil
Drew Cumming

Sleep & Neurodevelopment Consortium

Greg Holmes
Deborah Hirtz
Susan Redline
Shaun Purcell
Mary Carskadon
David Gozal
Ruth Benca
Leila Tarokh
Kathleen Merikangas
Peter Davis
Kiran Maski
Anne Marie Morse
Mirjana Savatic
Dan Glaze
Matt McGinley
Rodney Samaco
Matt Mahoney

IRP, NIMH

Maryland Pao
Susan Amara
Audrey Thurm
Cristan Farmer
Paul Grant
Tom Gaughan
Riley Kessler



DISCLOSURE SLIDE

No funds received at NIH from Pediatric Epilepsy Research Foundation

NIMH Intramural Research Program has a Memorandum of Understanding pending with BEL

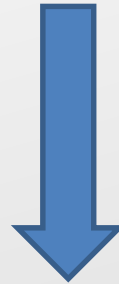


Sleep,
Neurodevelopment
& EEG Biomarker
Research in
Intramural NIMH



GOAL

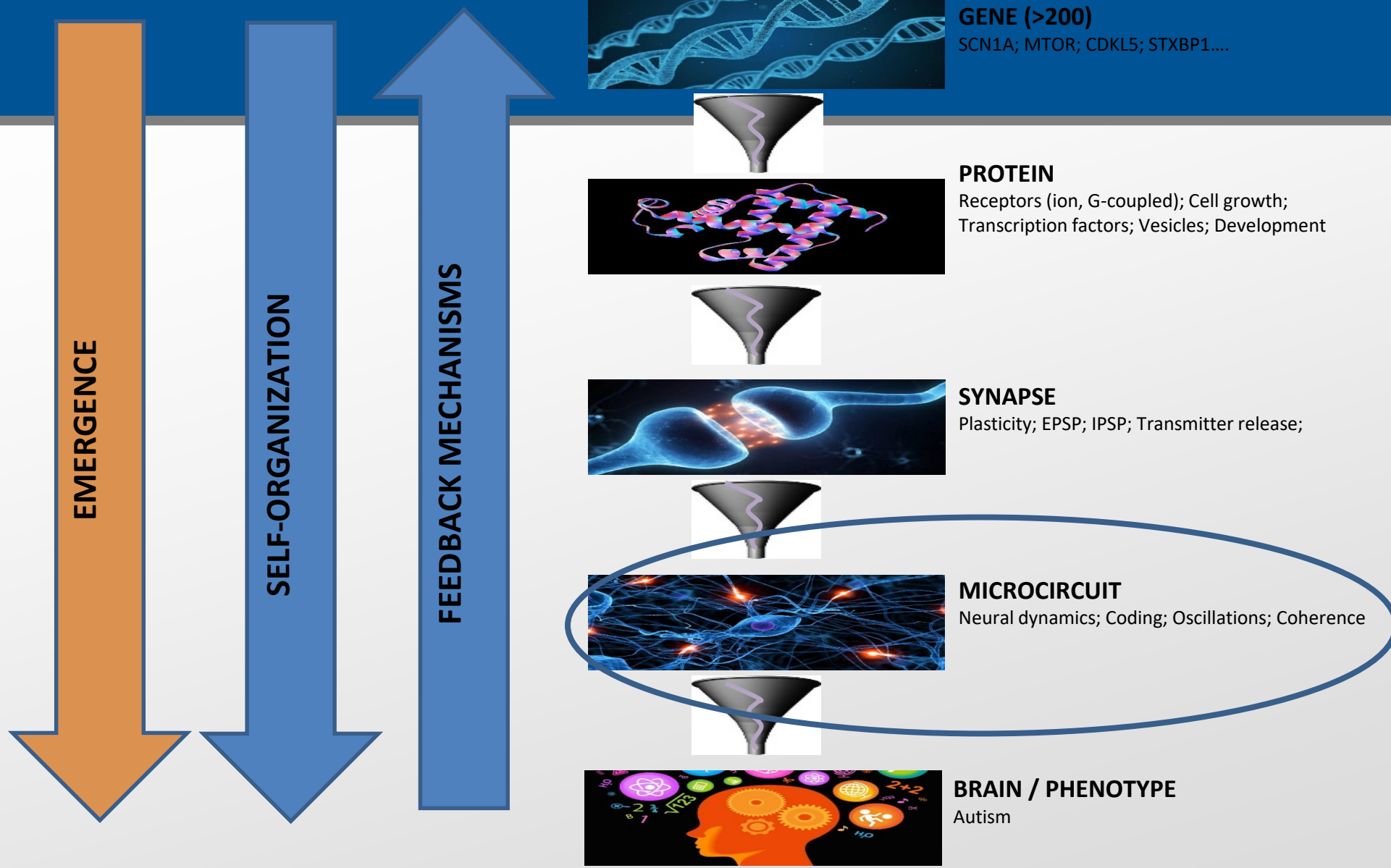
The creation of predictive algorithms of sleep metrics to aid in the establishment of optimal intervention points and potentially minimize negative outcomes



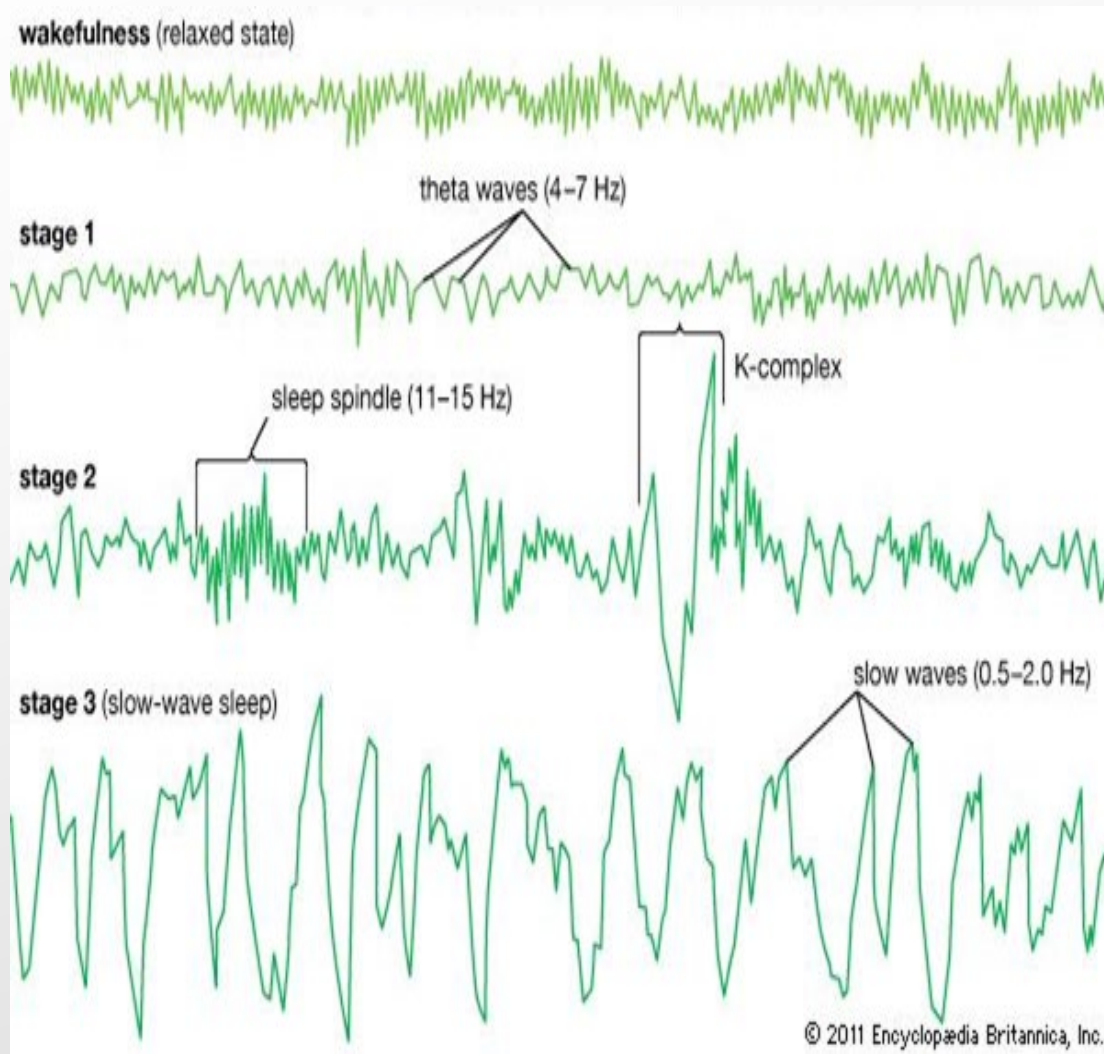
How do we measure/analyze sleep disturbance?

- Subjective Complaint
 - Questionnaires, parent report
- Objective Measurements
 - Actigraphy
 - activity as proxy for sleep/wake cycle
 - Polysomnography
 - integrates physiology, sleep stages, latencies, ultradian rhythms, **oscillatory information**





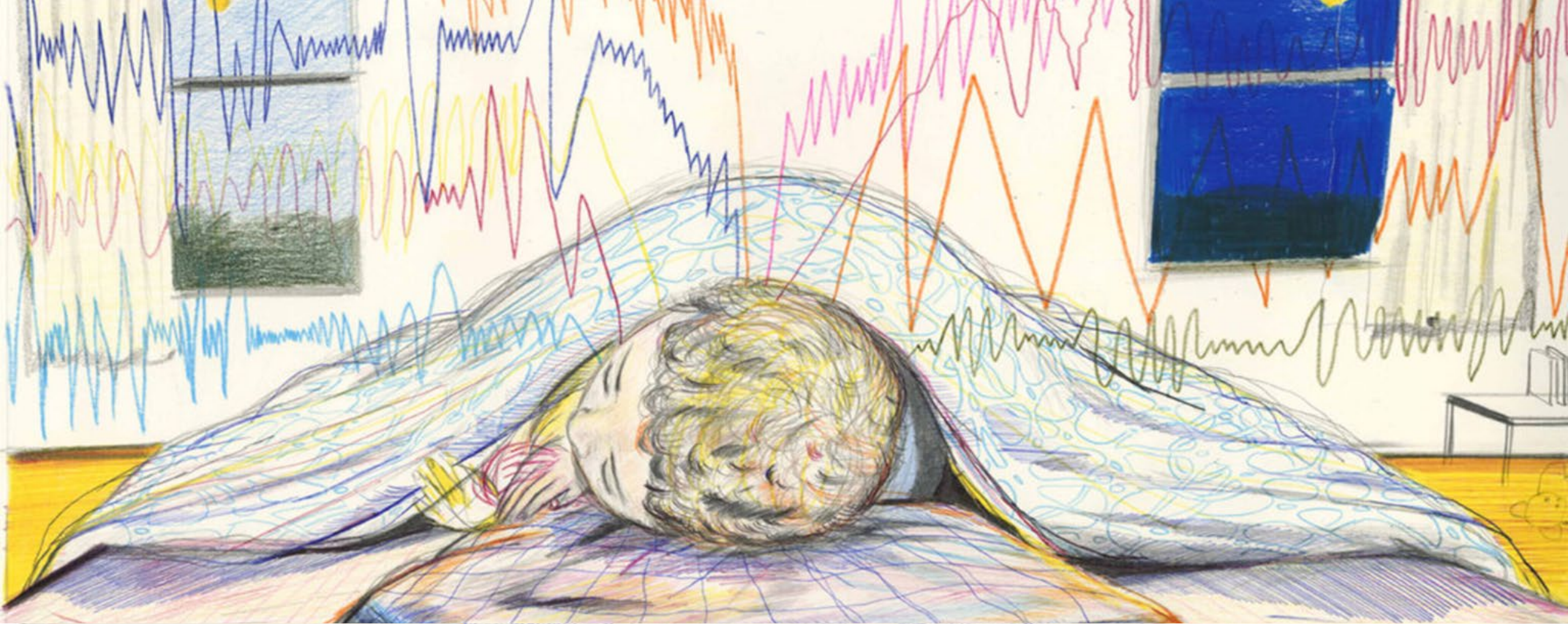
Sleep Electrophysiology Metrics



Architecture: Distribution of sleep stages

Power: Strength of signal as a function of frequency

Coherence: Functional connectivity between brain regions



<https://www.spectrumnews.org/news/cracking-autisms-sleep-conundrum/>

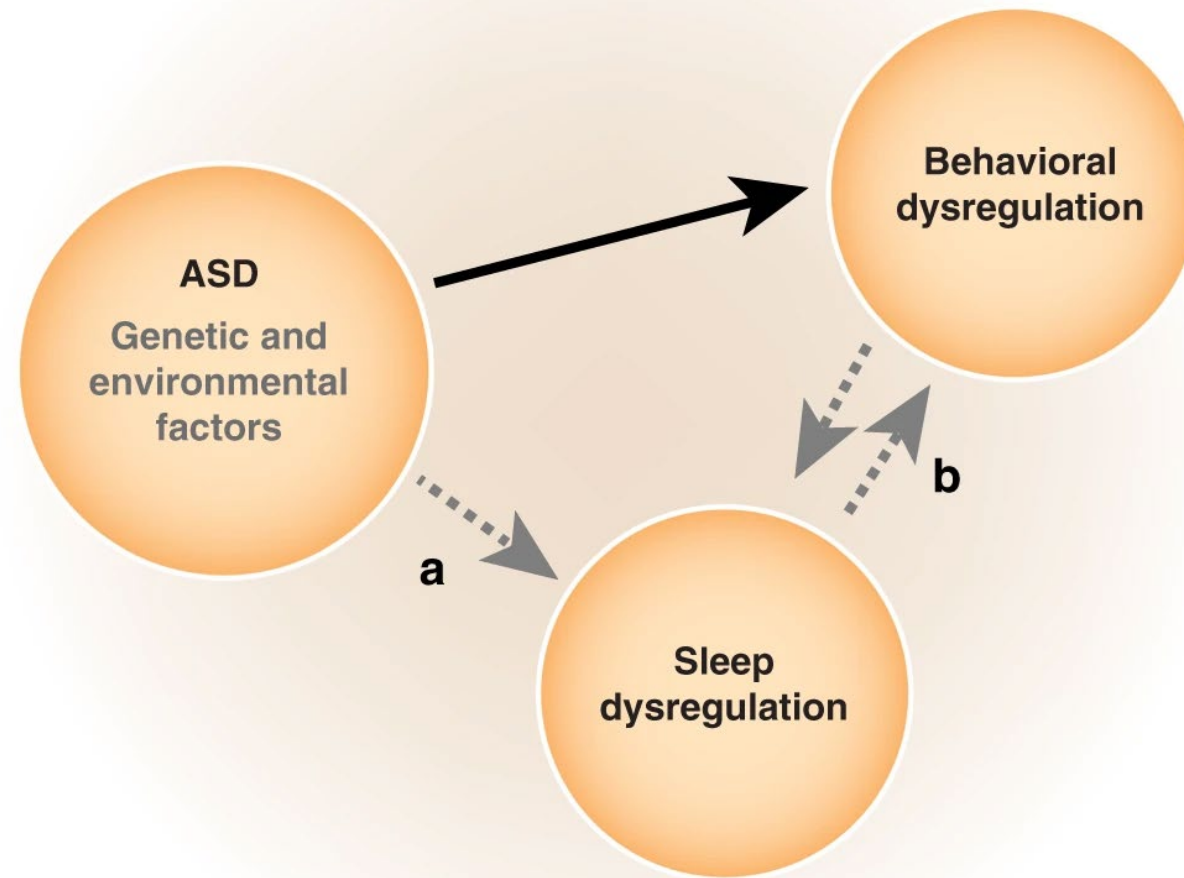
ILLUSTRATIONS BY YANN KEBBI

NEWS

Cracking autism's sleep conundrum

BY CHLOE WILLIAMS / 25 FEBRUARY 2022

What do abnormal sleep metrics reflect?



Missig, G et al Neuropsychopharmacol. 45, 90–103 (2020) doi:10.1038/s41386-019-0409-5



How do we move forward?

- **Consensus Building**
- **Sleep Data Repositories**
- **Investment in Infrastructure**



Consensus Building

Sleep & Neurodevelopmental Workshops at NIMH Intramural Research Program

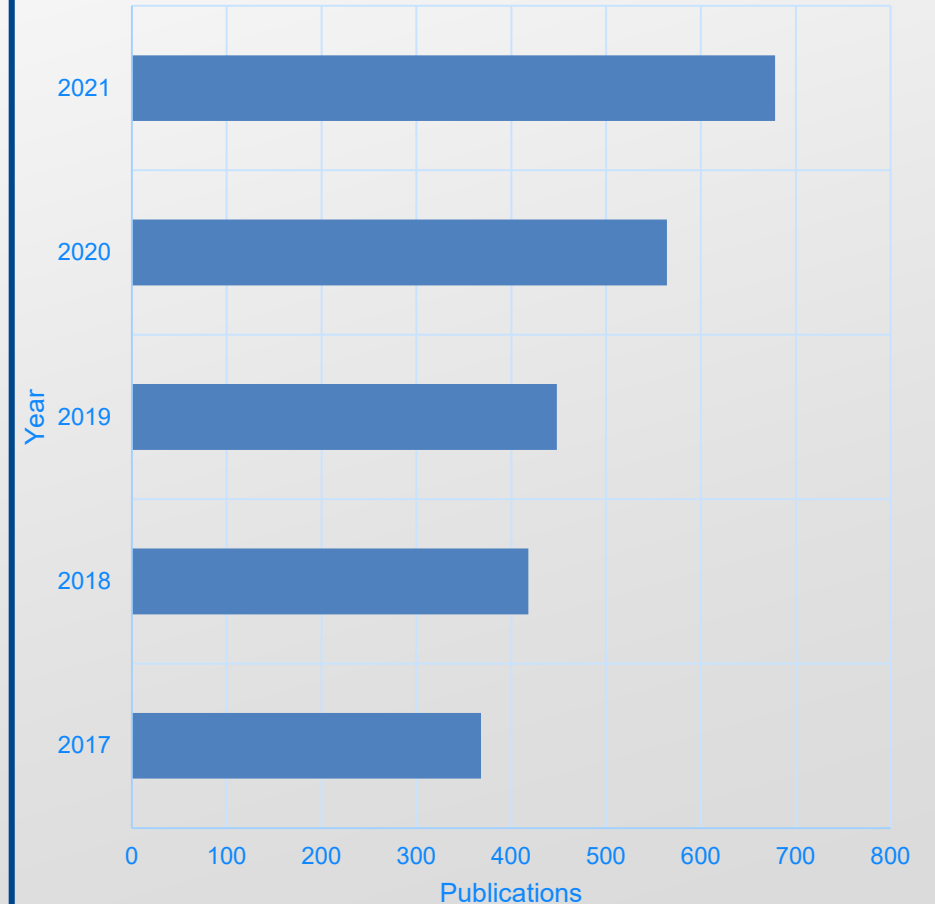
2014→Data Gaps

2017→Infrastructure

2018→Translation

2021→The Earliest Years

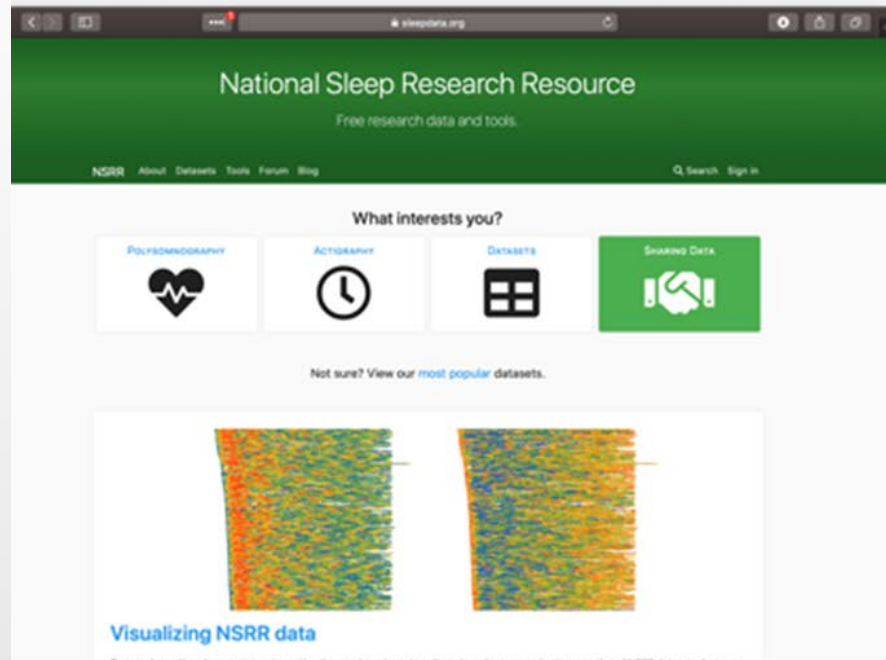
NDD and Sleep Publications by Year



Repository Identification & Collaboration

National Sleep Research Resource

A community resource to deposit and access primary sleep data including physiological signals



<http://sleepdata.org>

Sleep Data: polysomnography and/or actigraphy and self-report measures (35,000 EDFs from 30,000 subjects)

Other Data: demographics, anthropometry, medical history, symptoms, cardiovascular health indices, lung function, blood pressure, blood biomarkers, cognitive tests, physical activity, health behaviors and medications.



Cleveland Children's
Sleep and Health Study

& growing...

Honolulu Asian American
Aging Sleep Study



National Institute
of Mental Health

Investment in Infrastructure



Sleep & Neurodevelopment Consortium

Electrophysiologic Sleep Phenotyping: ESP

A Longitudinal, Prospective Study of Sleep & Neurodevelopment



Artist: Madison Hueston, Charles Herbert Flowers High School

Demographic, behavioral, genetic* and other biological, psychosocial and lifestyle data collected contemporaneously to EEG signatures

**In collaboration with*

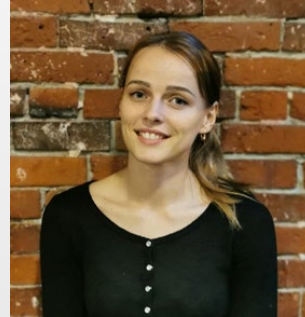
- NIAID Centralized Sequencing Protocol
- NIMH Repository and Genomics Resource



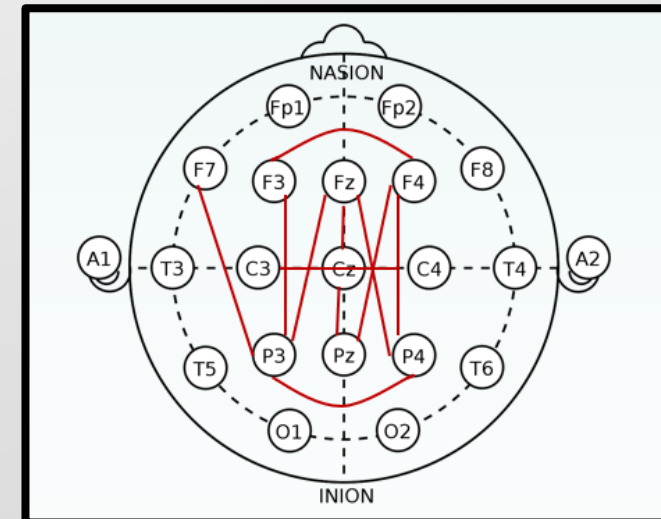
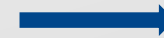
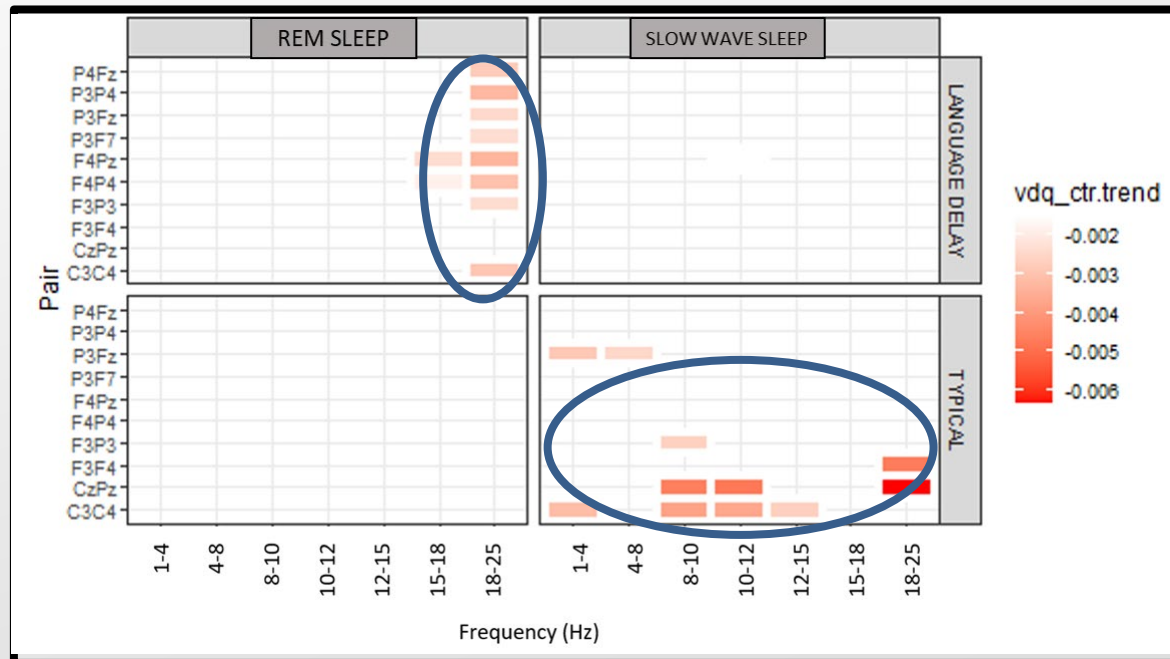
Unpublished Data: Toddler Protocol

- Relationship between verbal scores and increased coherence in REM and Slow Wave Sleep
- Differences in coherence patterns vary by developmental group

Demographic variables	Language Delayed (LD)		Typically Developing (TD)	
	Baseline	Follow-up	Baseline	Follow-up
N total	17	11	39	23
N (analytic)	16	11	38	23
Age, years M (SD)	1.64 (0.11)*	3.19 (0.28)	1.43 (0.25)	3.05 (0.20)
Age range, years	1.48- 1.85	2.82-3.82	1.05- 1.78	2.26-3.34
Sex (F)	6	5	15	8

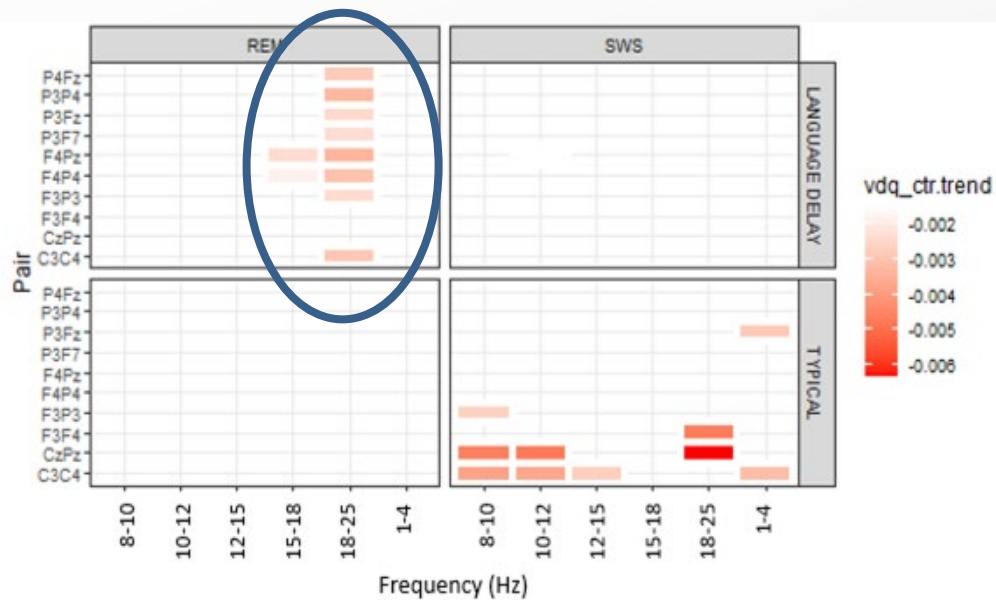


Natalia Kozhemiako



Xinyi Hong





Protocol
Development
Standard Setting

Data
Collection

Data
Archiving &
Analysis

Data Sharing



Full Site Possibilities



- POC devices & in-lab validation
- Circadian alignment in relation to oscillatory parameters
- Social determinants and oscillatory sleep metrics
- GABA-ergic dysgenesis in NDDs epilepsy and sleep dysfunction biomarkers: rhythmopathies
- Maturation of REM atonia

Ending Thoughts...

- Sleep Neurophysiology is Underexplored for Behavioral Trajectories
- Convergence Science is the Model for moving forward
- **Data Libraries of Normative Data during Development needed**

