



Business **Cooperative Research** Centres Program

Understanding the biological and behavioural attributes leading to sleep difficulties in children on the autism spectrum

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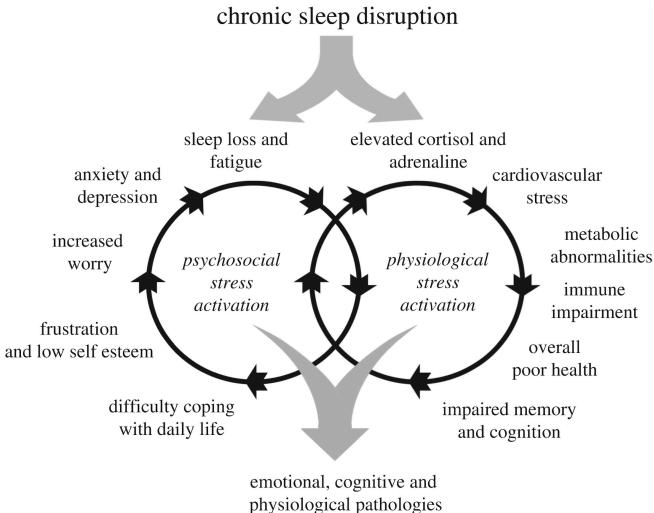
Sleep

- Recognised as a fundamental contributor to health and well-being outcomes
- A highly complex state making sleep vulnerable to disruption
- Sleep arises from interactions between multiple
 - Brain regions
 - Neurotransmitter pathways
 - Hormones





Sleep disturbance





Sleep disturbance

emotional	cognitive	physiology and health
increased	impaired	increased risk
fluctuations in mood	cognitive performance	day time sleepiness
irritability	ability to multi-task	micro-sleeps
anxiety	memory	cardiovascular disease
loss of empathy	attention	altered stress response
frustration	concentration	altered sensory thresholds
risk-taking and impulsivity	communication	infection, lowered immunity
negative salience	decision-making	cancer
stimulant use (caffeine)	creativity and productivity	metabolic abnormalities
sedative use (alcohol)	motor performance	diabetes II
illegal drug use	dissociation/detachment	depression and psychosis



R.G Foster. Sleep, circadian rhythms and health. Interface Focus 2020

Sleep disturbance in children on the spectrum

What does it look like?

- Bedtime resistance
- Sleep latency; difficulties initiating sleep
- Waking after sleep onset
- Multiple night arousals; poor sleep maintenance
- Short sleep duration
- Early morning wakening



Sleep disturbance in children on the spectrum

What does it look like?

- 80% of autistic children aged 2 to 5 years have disrupted sleep*
- Autistic children are twice as likely to have sleep issues as typical children or those with other developmental conditions *
- Early sleep problems are a predictor of repetitive behaviours later in childhood**
- Sleep problems predict later inattention and hyperactivity. ***
- Associated with daytime problem behaviours****



*Reynolds AM et al. *Pediatrics*. 2019;143(3):e20180492 **MacDuffie KE et al. *J Autism Dev Disord*. 2020 ***Mazurek MO et al. *J Autism Dev Disord*. 2019;49(5):2101–2115 ****Sikora DM et al. *Pediatrics*. 2012;130 Suppl 2:S83–S90

Sleep disturbance in children on the spectrum

What to do?

- Behavioural strategies
- Bedtime routines
 - Avoid stimulating foods and drink before bedtime
 - Avoid video games and TV (Blue Light)
- Sleep environment (temperature, sound, light)
- Parent-based sleep education Melatonin

Where to start?

- Behaviour
- Environment
- Biological

Research aims

- 1. Define sleep difficulties in children on the autism spectrum aged 2-17 years, including sleep latency, waking after sleep onset and sleep duration .
- 2. Evaluate the relationship between sleep difficulties and clinical phenotype including gender, autism profiles, cognitive level, sensory profile, gastrointestinal dysfunction, epilepsy, and psychiatric co-morbidities such as anxiety.
- 3. Measure melatonin and melatonin metabolites in urine samples and identify genetic influences that might contribute to abnormal melatonin metabolism in children on the autism spectrum.
- 4. To evaluate the interactions between sleep and melatonin profile and phenotypic presentation.



Recruitment

- Access request to The Australian Autism Biobank
- ETHICS: UNSW HREC HC190923
- Children aged between 2-17 with a diagnosis of autism, their non-autistic siblings and typically developing healthy controls.



Measures

- Childhood Sleep Habits Questionnaire
- ADOS
- Cognitive assessment (Mullen or WISC-IV)
- Sensory profile
- Adaptive Behaviour (Vineland-II)
- Family medical and social history



Analysis

- Descriptive statistics for demographics of participant groups (gender and age) and independent variables and frequency distributions for the various variables.
- Sleep profiles based on the key domains screened in the CSHQ compared between children on the autism spectrum, non-autistic siblings and control groups.
- Sleep onset delay, sleep duration, and sleep total subscales will be used to identify children on the autism spectrum with a sleep problem and those with no sleep problem.
- Correlations between these sleep variables, behavioural attributes and genetic influences contributing to abnormal melatonin metabolism and metabolite concentrations.



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References

Foster, RG. Sleep, circadian rhythms and health. Interface Focus 2020

MacDuffie KE, Munson J, Greenson J, et al. Sleep Problems and Trajectories of Restricted and Repetitive Behaviors in Children with Neurodevelopmental Disabilities [published online ahead of print, 2020 Mar 5]. *J Autism Dev Disord*. 2020;10.1007/s10803-020-04438-y. doi:10.1007/s10803-020-04438-y

Mazurek MO, Dovgan K, Neumeyer AM, Malow BA. Course and Predictors of Sleep and Co-occurring Problems in Children with Autism Spectrum Disorder. *J Autism Dev Disord*. 2019;49(5):2101–2115. doi:10.1007/s10803-019-03894-5

Reynolds AM et al. Sleep Problems in 2- to 5-Year-Olds With Autism Spectrum Disorder and Other Developmental Delays. *Pediatrics*. 2019;143(3):e20180492. doi:10.1542/peds.2018-0492

Sikora DM, Johnson K, Clemons T, Katz T. The relationship between sleep problems and daytime behavior in children of different ages with autism spectrum disorders. *Pediatrics*. 2012;130 Suppl 2:S83–S90



Thank you

Questions?

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Autism CRC is the world's first national, cooperative research centre focused on autism. We are taking a whole-of-life approach to autism focusing on early years, school years and adulthood.