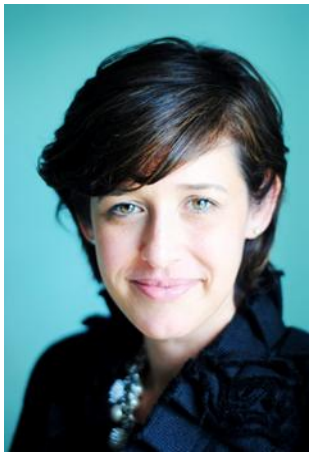
RESEARCH ROUNDUP
NEUROPSYCHOLOGY



Karin S. Walsh, Psy.D.
Children's National Hospital
The George Washington University School of Medicine
Washington, DC

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Agenda

- Summary of recent cognitive research studies
- Future cognitive research studies

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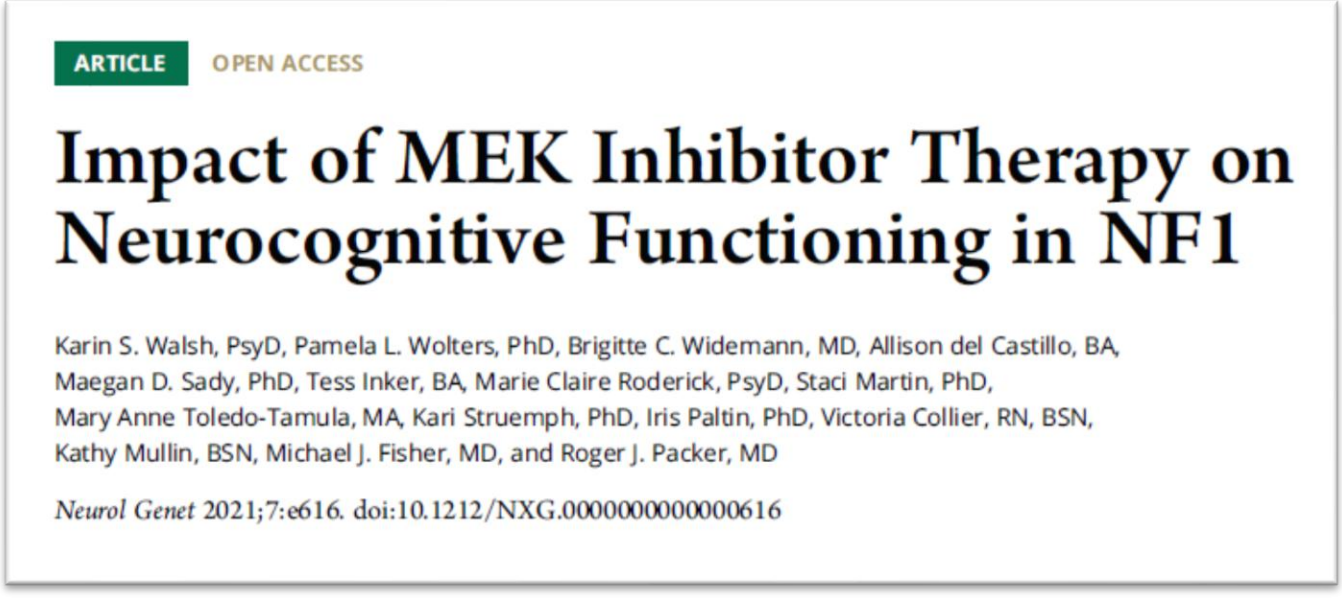
Cognitive Changes during treatment with a MEK inhibitor



ARTICLE OPEN ACCESS

Impact of MEK Inhibitor Therapy on Neurocognitive Functioning in NF1

Karin S. Walsh, PsyD, Pamela L. Wolters, PhD, Brigitte C. Widemann, MD, Allison del Castillo, BA, Maegan D. Sady, PhD, Tess Inker, BA, Marie Claire Roderick, PsyD, Staci Martin, PhD, Mary Anne Toledo-Tamula, MA, Kari Struemph, PhD, Iris Paltin, PhD, Victoria Collier, RN, BSN, Kathy Mullin, BSN, Michael J. Fisher, MD, and Roger J. Packer, MD

Neurol Genet 2021;7:e616. doi:10.1212/NXG.0000000000000616

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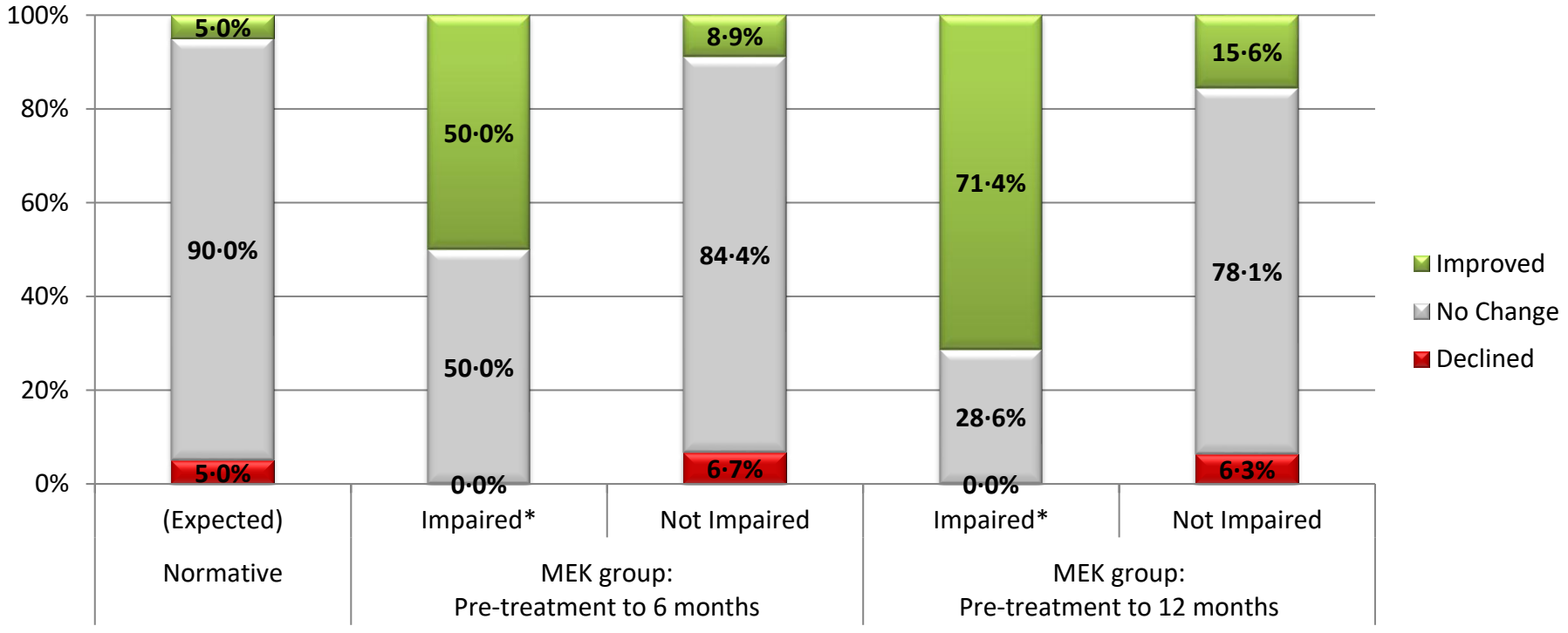
Parent-Rating Executive Function



BRIEF MCI = Behavior Rating Inventory of Executive Functioning, Metacognition Index; RCI = Reliable Change Index; MEK = Received Mitogen-activated protein kinase inhibitor

*Significantly different from Normative (Expected) proportions using 2-tailed 90% CI

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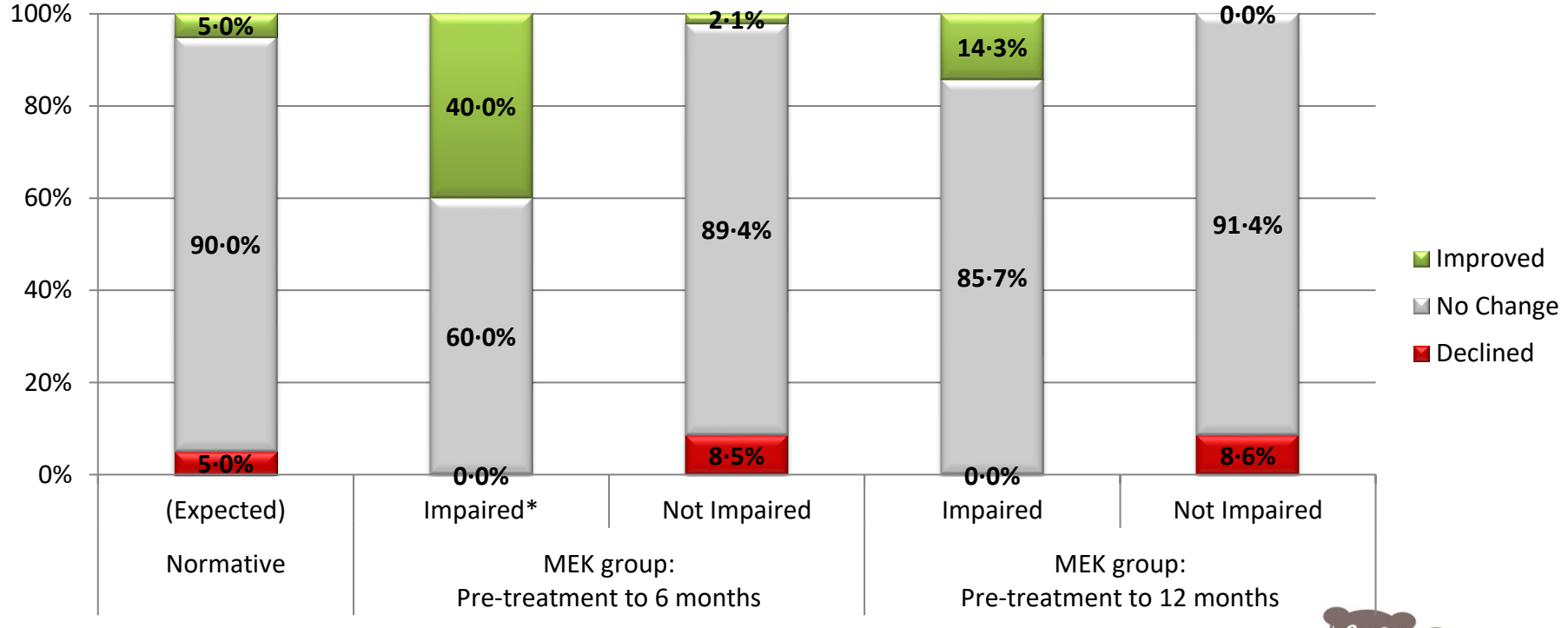
Working Memory Performance



ONB = One-Back Cogstate; RCI = Reliable Change Index; MEK = Received Mitogen-activated protein kinase inhibitor
*Significantly different from Normative (Expected) proportions using 2-tailed 90% CI

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Summary of Results

- First human trial investigating MEK inhibitors on cognitive outcomes in NF1
- Does not appear to be neurotoxic
- Current results highlight a potential for targeting this pathway to address cognitive deficits in NF1
- Those with pre-treatment impairments show greater improvement, more evident with more time on treatment
- Current and future randomized clinical trials will expand our understanding of these findings

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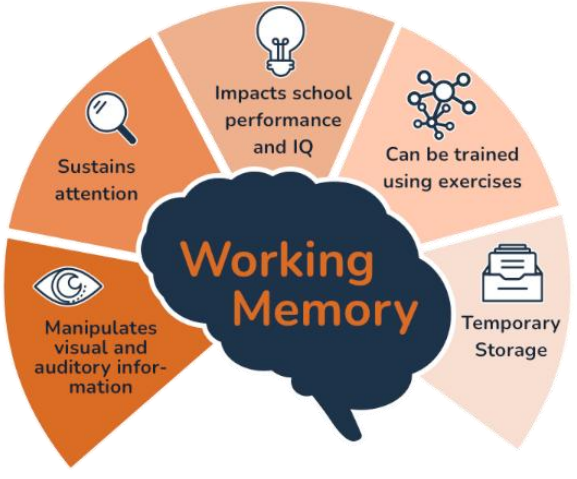
Cognitive Overload Study

- Aims:
  - To study the impact of cognitive load on performance in children with NF1
- Cognitive load defined as increased demands for working memory and inhibition

Results

- Children with NF1 show poorer performance in response to increased cognitive load
  - Less accurate and less consistent
  - Difficulty adjusting to increased demands
- This can interfere with school and social functioning
- Working memory may be a target for intervention



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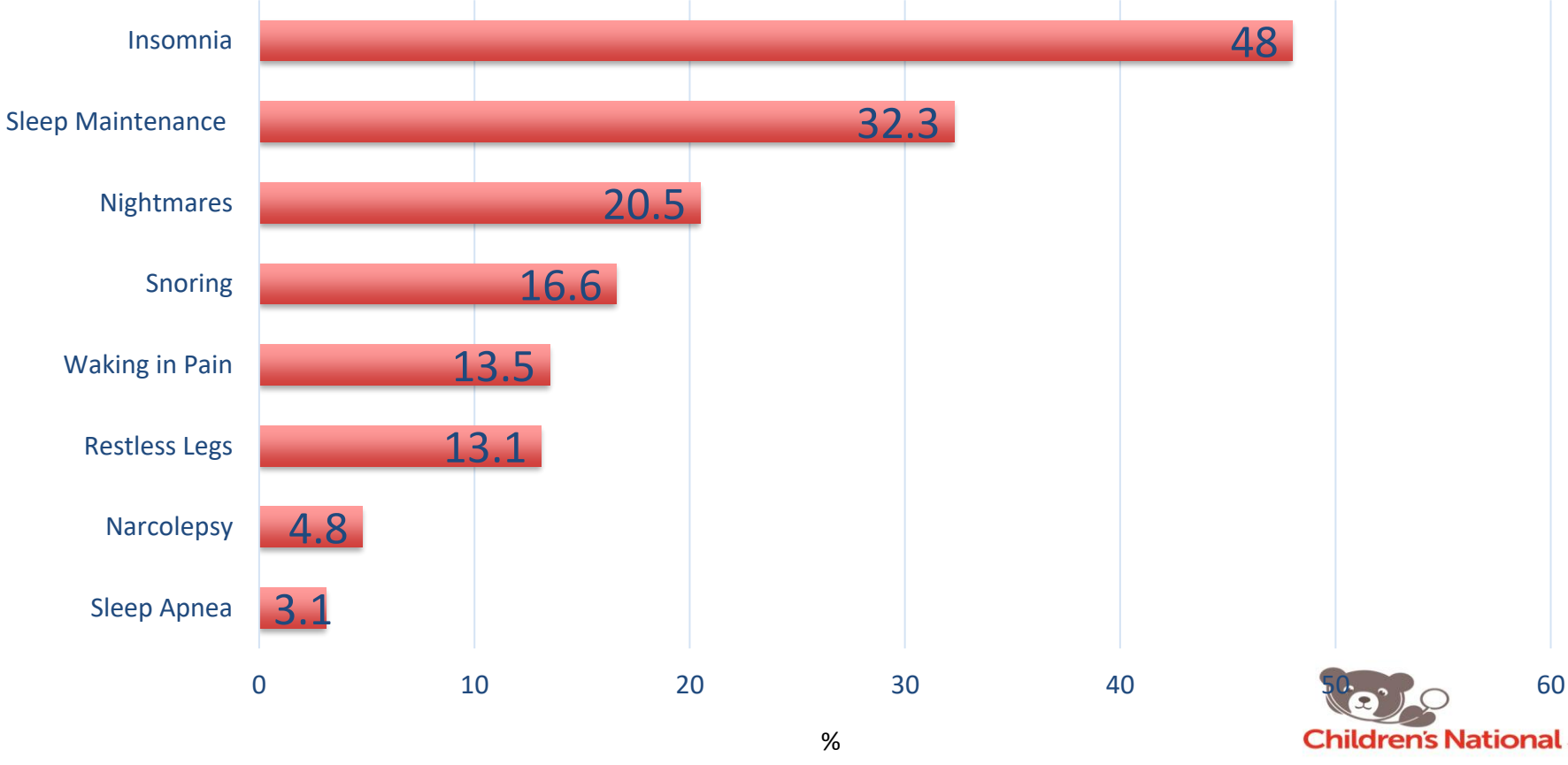
Sleep and Learning Study (DREAM)

- Aims:
  - To document the amount and type of sleep problems in people with NF1 (Phase I)
  - To see if there is a relationship between sleep problems and learning in children with NF1 (Phase II)

Rates of Sleep Disturbances



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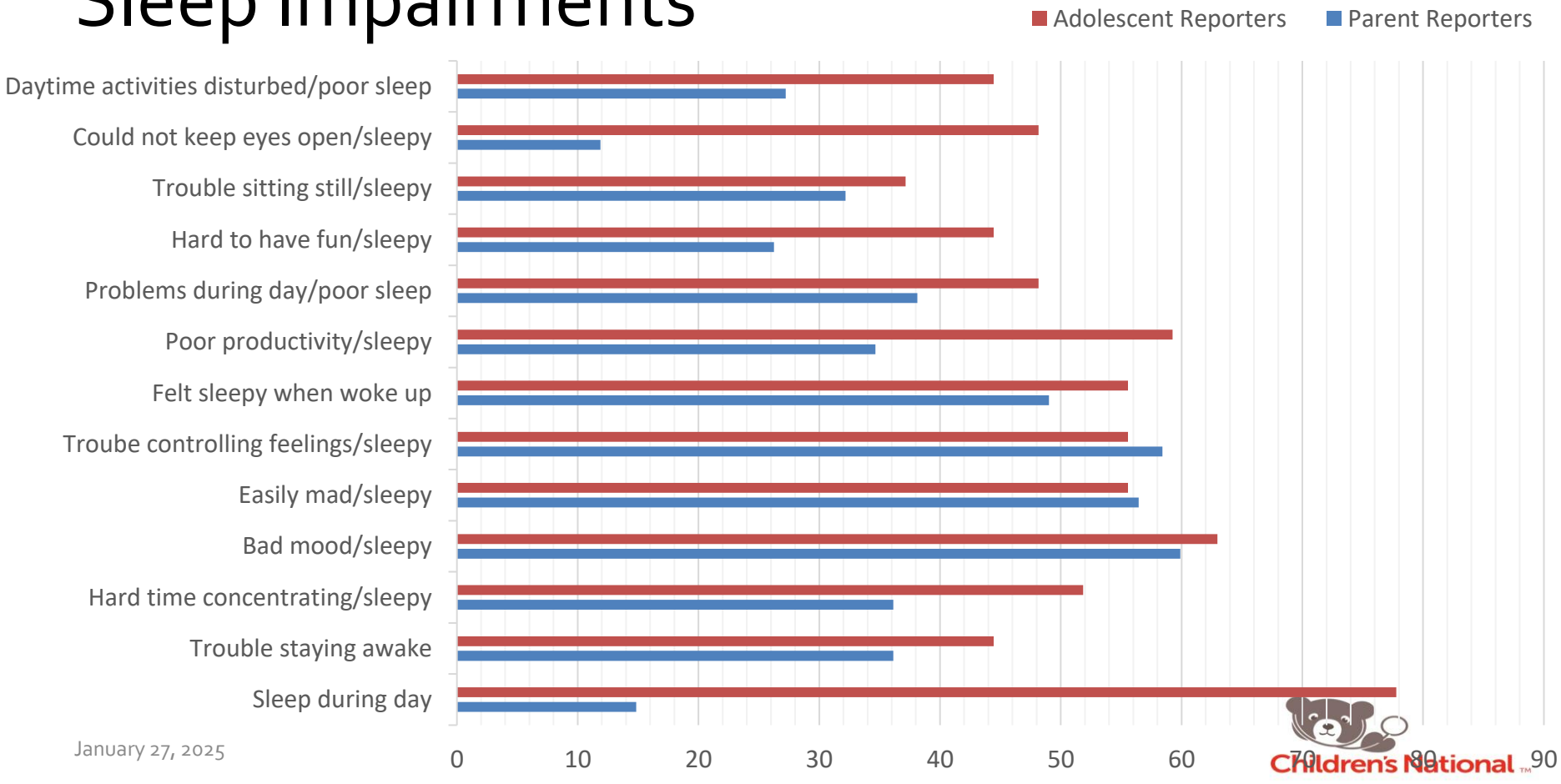
Sleep Impairments



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Other Sleep Related Factors

14% of children have met with a sleep specialist. To address sleep difficulties, 32.8% of participants take melatonin, 4.3% take other sleep medication.

A large portion of children and adolescents with NF1 report watching television (78.2%) or using a device (75%) before falling asleep.

Some children report daily caffeine intake (17%) with just 1.3% consuming 3 or more drinks per day.

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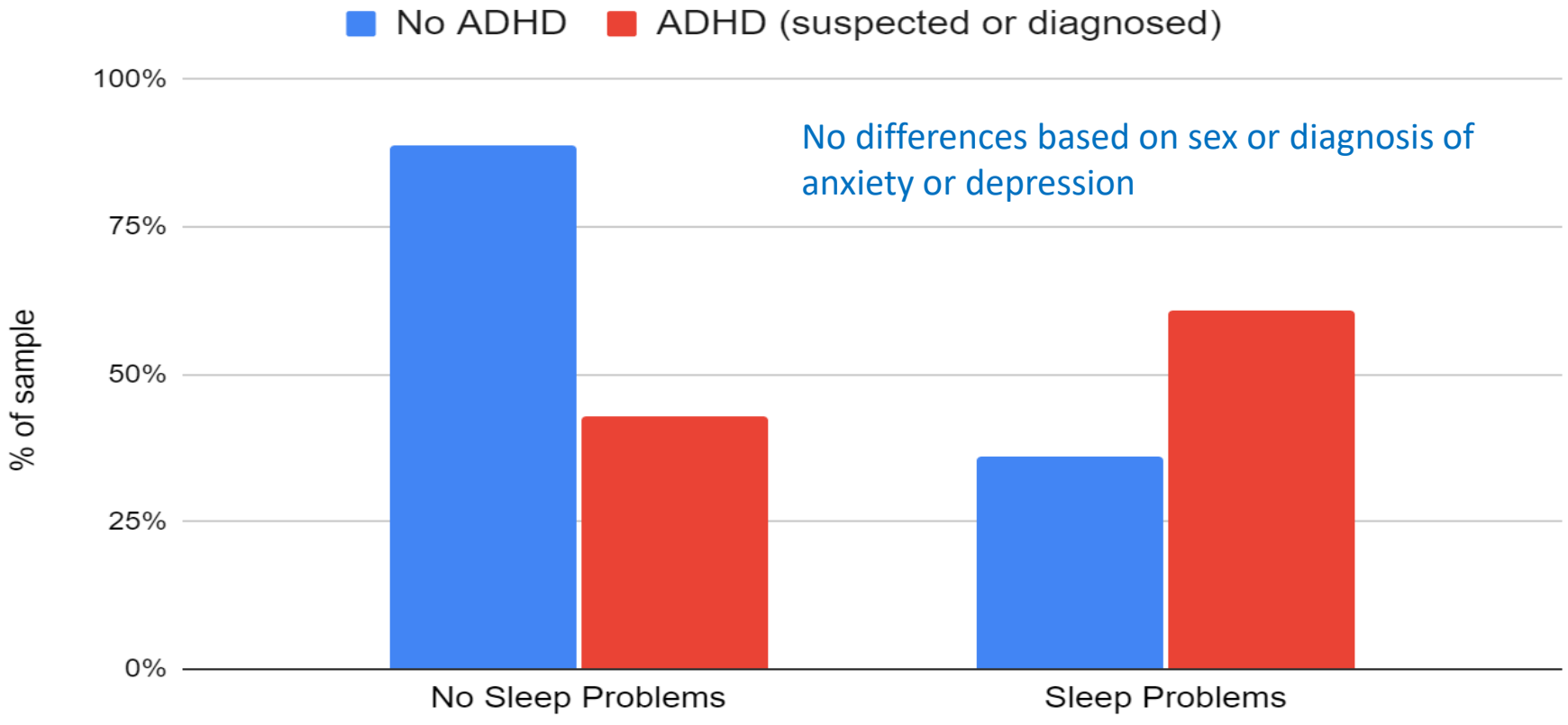
Sleep Problems and ADHD



Summary

- Parents of children and adolescents with NF1 report sleep disturbance and impairment, attention, academic, and emotional difficulties.
- Adolescents report higher rates of sleep impairment, suggesting sleep impairment difficulties may increase over time.
- Many problems overall were reported before going to sleep including media use before bed, sleep avoidance, and problems sleeping alone. Other frequent problems included restless and inconsistent sleep and morning fatigue.
- Device use at bedtime is common. Blue light contributes to sleep impairment
- It appears that children with NF1 & ADHD having greater reported sleep problems

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Unstuck and On Target (UOT) Executive Function Intervention Pilot

- 20-week group intervention
- Aims: establishing how

  feasible and acceptable the intervention was for families and children

- Online for Parents:
  - https://www.unstuckandontarget.com/e-unstuck

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Parent Satisfaction

- 75% of parents report changes in their child's behavior, attitude, or emotions following participation in UOT.
- 100% reported changes in their child's flexibility and planning skills.

	How helpful were the following elements:							
	Skills taught	Talking with a clinician	Practice activities	Group format	Applying skills in daily life	Using skills, strategies, or vocab	Did UOT help you and your child?	Did your child learn anything?
Average Parent Rating	4.5	5	3	5	3.5	4.5	4.25	4.5

Summary

Intervention was feasible: 95-100% attendance with no dropouts

Intervention was seen as beneficial

Challenges with applying learning in home and other settings (generalizing)

Ongoing and Upcoming Studies

Sleep and Learning Study (DREAM)

Executive Function Intervention for children with brain tumors

Translational models in cognitive research

THANK YOU!

Dr. Thomas

Dr. Cap

Dr. Gioia

Rebecca Levitt

Meredith Goyette

To all the families and children who have contributed to this work by taking time out of their lives to volunteer to participate in our research.

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