



Modifiable lifestyle factors to support neurodevelopment in individuals with FASD

Blake Gimbel, PhD

Nationwide Children's Hospital & The Ohio State University

Jeff Wozniak, PhD

University of Minnesota

Learning Objectives

1. Identify the role of modifiable lifestyle factors in supporting neurodevelopment
1. Understand the relevance of lifestyle factors to optimizing neurodevelopment in individuals with FASD
1. Appreciate the need for cost effective and accessible interventions to support neurodevelopment in individuals with FASD

Modifiable lifestyle factors

- Non-medical
- Broadly applicable
- Habit/behavior changes
- Evidence-based
- Benefit mood, cognition, brain function

Nutrition



Nutrition is foundational to brain health



- Building blocks for brain development
- Deficiencies have lasting consequences
- Valuable opportunity for intervention

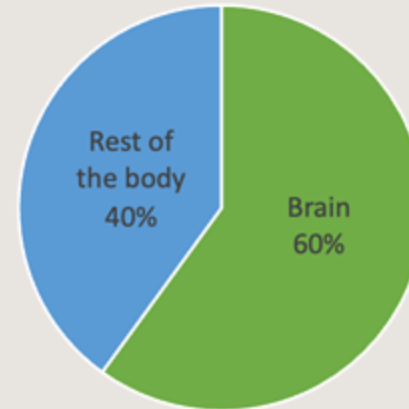


Nutrition is foundational to brain health

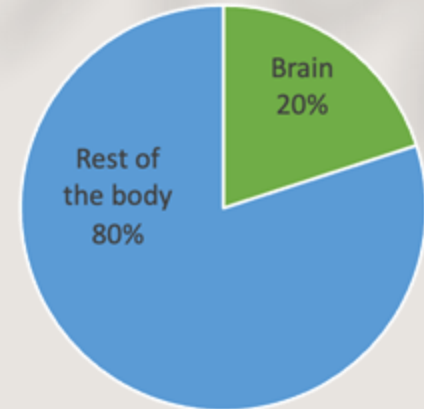


- Brain development is a highly metabolic process
- Growth relies on nutrients that support energy metabolism
 - Oxygen, glucose, protein, iron, copper, iodine

Percent Caloric Consumption:
Children



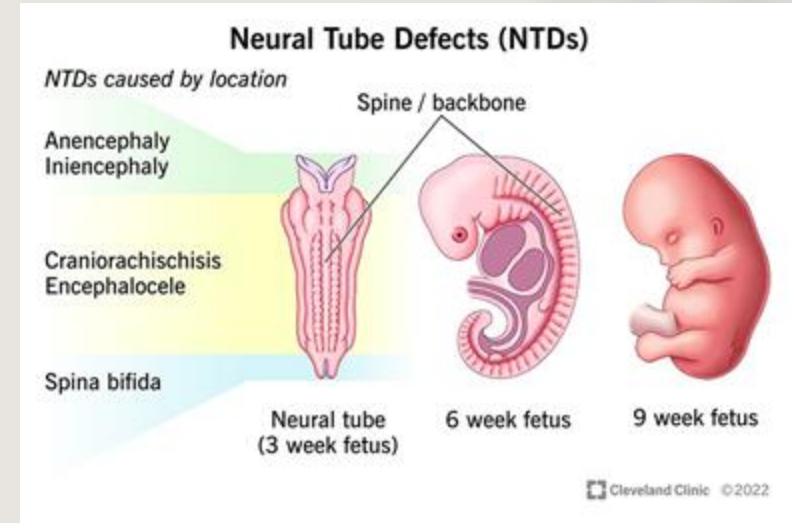
Percent Caloric Consumption:
Adults



Nutrition is foundational to brain health



- Ex. Folate deficiency during development leads to neural tube defects



Nutrition is foundational to brain health



- Ex. Iron deficiency during brain development leads to lower IQ, attention problems, memory deficits, & learning problems



Nutrition is foundational to brain health



- Ex. Choline deficiency during brain development directly impacts formation of the hippocampus and, as a result, memory functioning



Nutrients that particularly affect early brain development and adult function



- **Macronutrients**

- Protein ^{1, 2}
- Fats (LC-PUFA) ^{1, 2, 3}
- Glucose ^{1, 2}

- **Micronutrients**

- Iron ^{1, 2, 3}
- Zinc ^{1, 2}
- Copper ^{1, 2}
- Iodine (Thyroid) ^{1, 2}

- **Vitamins/Cofactors**

- B vitamins (B6, B12₁)
- Vitamin A
- Vitamin K
- Folate ^{1, 2, 3}
- Choline ^{1, 2, 3}

1 Exhibits critical/sensitive period for neurodevelopment

2 Early deficiency results in long-term dysfunction

3 Evidence for epigenetic mechanism

Alcohol impacts nutrition during pregnancy



- Alcohol consumption during pregnancy:
 - Associated with poor diet
 - Interferes with nutrient absorption
- PAE combined with inadequate nutrition is especially harmful to brain development



Nutrition as an intervention during pregnancy



- Nutritional supplementation during pregnancy can offset impacts of PAE
- Ex. Prenatal choline/multivitamin supplementation during alcohol exposed pregnancies found to support:
 - Infant growth
 - Early childhood cognitive development



Ex. South African maternal choline supplementation trial

- Randomized, double-blind, placebo-controlled trial
 - 50 infants with heavy PAE
 - Brain MRI at 2.8 weeks postpartum
 - Recognition memory assessed at 12 months
- Choline group showed larger brain volumes vs placebo
- Larger brain volumes associated with improved memory performance



Alcohol impacts nutrition during childhood



- During childhood, nutrient intake continues to be critical for brain development
- Children with FASD have food sensitivities and eating patterns that can impact nutrition



Alcohol impacts nutrition during childhood



- Children with FASD have lower quality nutrient intake
 - 90% inadequate fiber
 - 97% inadequate n-3 fatty acids
 - 48% inadequate n-6 fatty acids
 - 84% inadequate choline
 - 32% inadequate iron



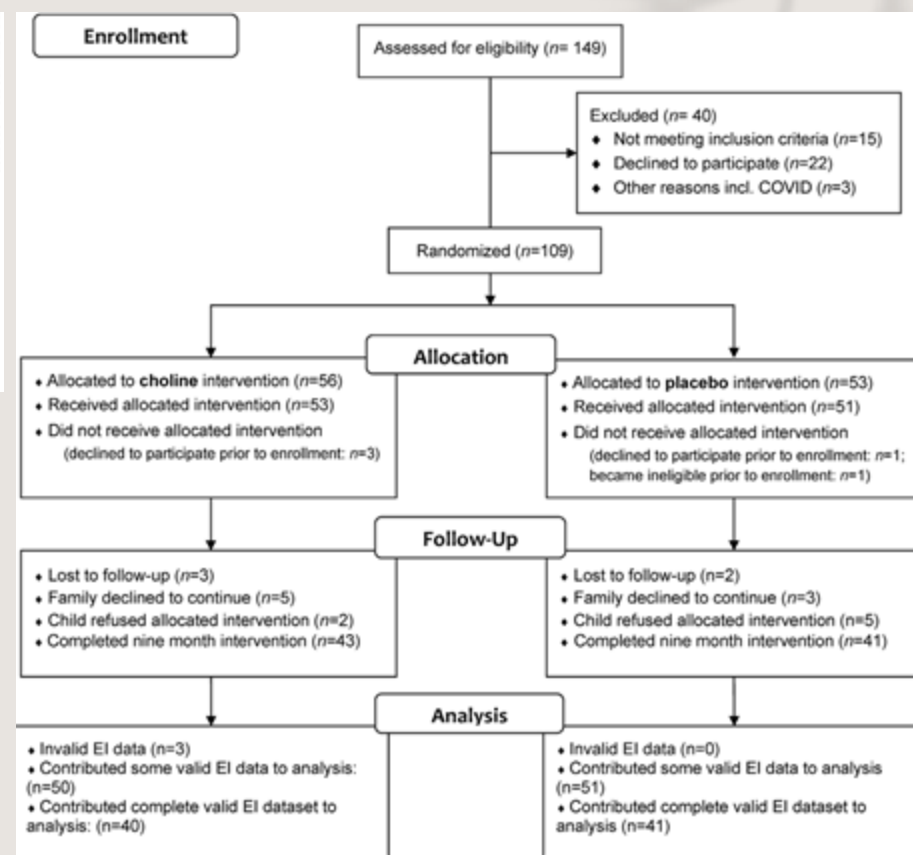
Nutrition as an intervention for children with PAE: University of Minnesota choline trials



- Nutritional supplementation during early childhood also confers important benefits
- Ex. Choline
 - Safe and well-tolerated
 - Provides benefits for hippocampal memory function in young children
 - Evidence for larger benefits over time in non-verbal IQ, attention, memory, executive functioning



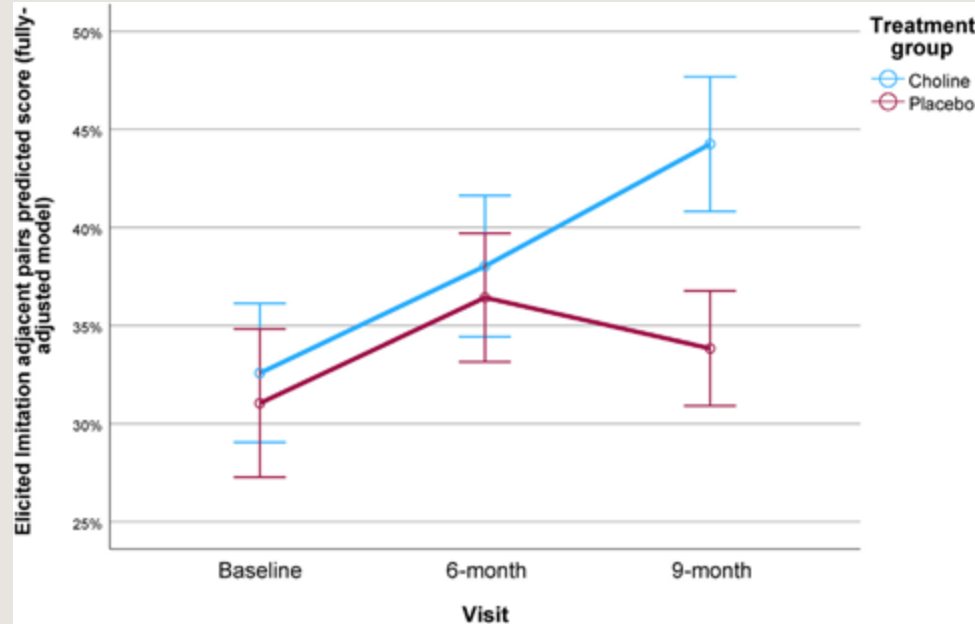
- Combined: 3 Randomized Controlled Trials between 2010 and 2021
 - Ages 2.5 to 5.9 years
 - 9-month duration
- Compared fixed 500 mg per day vs 22 mg/kg vs placebo



Original Research Article

Choline enhances elicited imitation memory performance in preschool children with prenatal alcohol exposure: a cumulative report of 3 randomized controlled trials

Jeffrey R Wozniak^{1,*}, Judith K Eckerle², Blake A Gimbel^{3,4}, Abigail M Ernst¹, Mary E Anthony¹, Kent A Tuominen¹, Erik de Water⁵, Steven H Zeisel⁶, Michael K Georgieff²



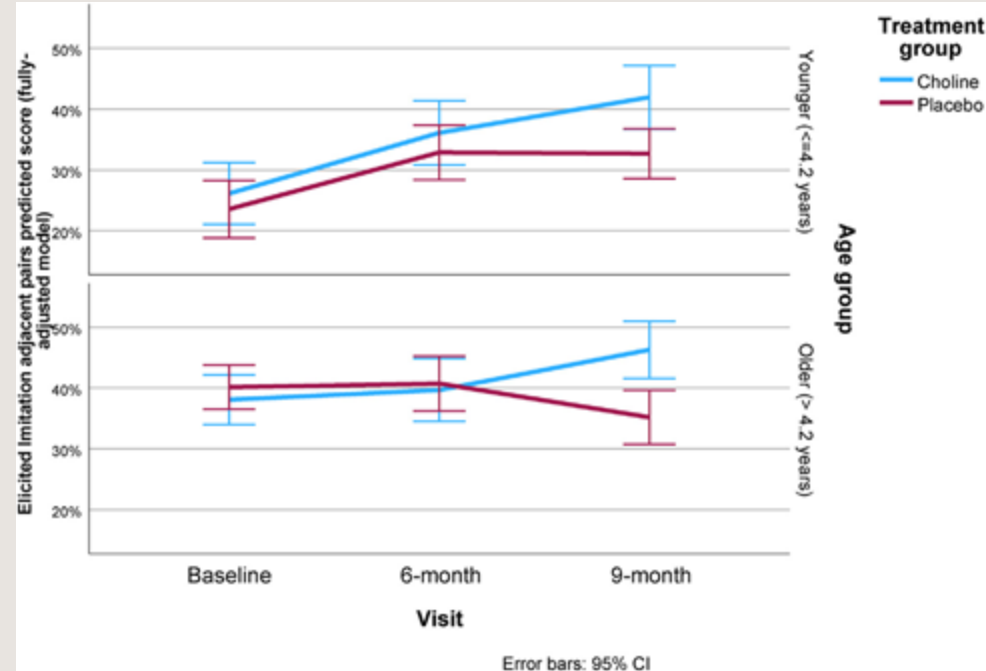
- Compliance was very good (78%)
- No adverse effects other than fishy odor (36% choline group vs. 8% placebo group)
- Fishy odor was higher for 500mg (57%) vs. weight-adjusted (11%)
- Sequential memory performance improvement favored choline (35.4%) vs. placebo (10.9%)

<https://doi.org/10.1016/j.ajcnut.2025.02.009>

Original Research Article

Choline enhances elicited imitation memory performance in preschool children with prenatal alcohol exposure: a cumulative report of 3 randomized controlled trials

Jeffrey R Wozniak^{1,*}, Judith K Eckerle², Blake A Gimbel^{3,4}, Abigail M Ernst¹, Mary E Anthony¹, Kent A Tuominen¹, Erik de Water⁵, Steven H Zeisel⁶, Michael K Georgieff²



- Younger age associated with greater improvement in memory performance
- No choline effect for IQ, executive functioning, or parent-reported behavior

<https://doi.org/10.1016/j.ajcnut.2025.02.009>

Evidence from related conditions



ADHD - Randomized Controlled Trials

Essential multi-nutrient supplementation

Clinician rated severity of symptoms:

- ↓ Emotion dysregulation
- ↓ Inattentive symptom

Vitamin D + Magnesium supplementation

Compared to placebo, treatment group showed:

- ↓ Internalizing difficulties score
- ↓ Peer conflict score

Everyday practical strategies: Nutrition



Serving Size of Meat and Fish



Photo: Vicky Wasik; Food Styling: Ola Wadley; Design: Kitchen
Visualization of serving size of meat and fish

- Incorporate foods that are high in Choline
 - **Salmon**, 3 ounces/85 grams: 187mg (34% DV)
 - **Hard boiled egg**, 1 large/50 grams: 147mg (27% DV)
 - **Roasted soybeans**, ½ cup/93 grams: 107mg (19% DV)
 - **Chicken breast**, 3 ounces/85 grams: 72mg (13% DV)
 - **Atlantic cod**, 3 ounces/85 grams: 71mg (13% DV)
 - **Ground beef**, 3 ounces/85 grams: 72mg (13% DV)
 - **Red potato with skin**, 1 large/299 grams: 57 mg (10% DV)

Supporting healthy eating in young children



- Early eating experiences shape eating habits later in life
 - Food preferences are strongly related to eating patterns - we like what we are most familiar with
 - Early and broad exposure to healthy foods is crucial for supporting lifelong healthy eating habits
 - From 4-24 months of age, 8-10 exposures to a single food increases acceptability

Supporting healthy eating in young children



- Strategies for picky eaters:
 - Model trying new foods
 - Provide choices
 - Pair new foods with familiar ones
 - Try foods with a variety of textures
 - Try something new, wait a few days, try it again
 - Make eating new foods a fun game!

Healthy eating as an adult

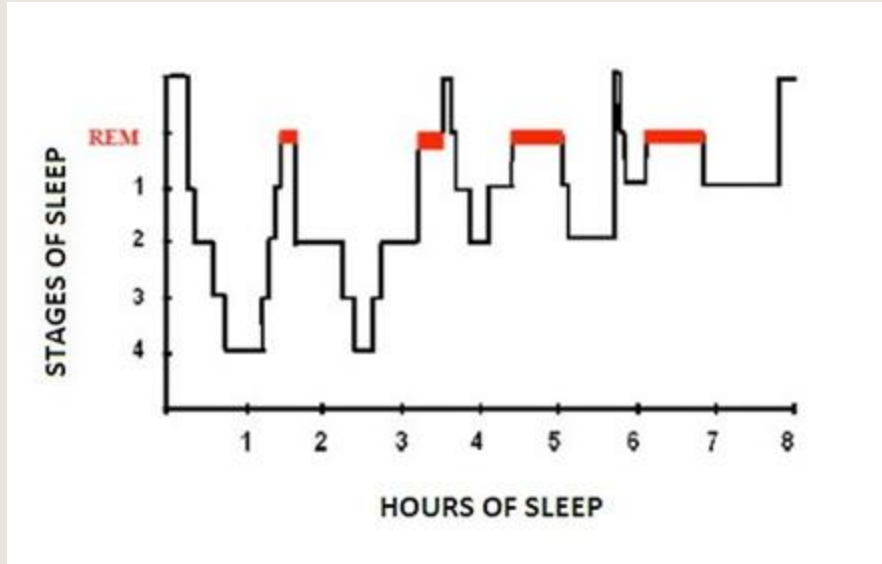
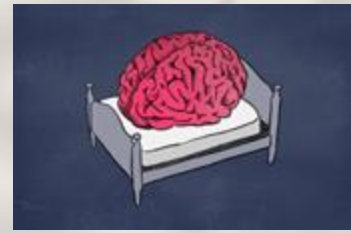


- Think small habit changes vs. drastic fads or diets
- Track eating for several days (e.g. cronometer.com, etc.)
 - Learn nutritional content
 - See your personal habits / patterns
- Think about portion sizes
- Plan shopping / meals; Cook
- Become aware of cues and alter them
- Eat food...not too much...mostly plants
- Slow your eating
- Avoid sugary beverages

Sleep

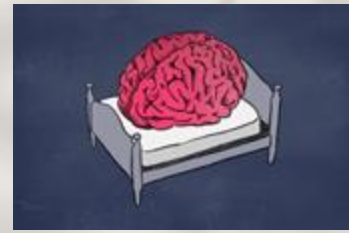


Sleep is critical for healthy brain function



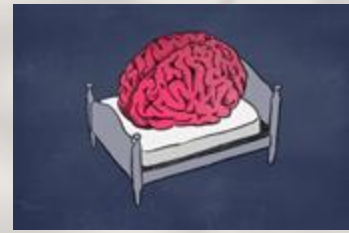
The sleep cycle, including the 5 stages of sleep

Sleep needs change over the lifespan



Group	Age	Recommended Sleep Per Night
Newborn	0-3 months	14-17 hour
Toddler	1-2 years	11-14 hours (including naps)
Preschool	3-5 years	10-13 hours (including naps)
School age	6-12 years	9-12 hours
Teenager	13-17 years	8-10 hours
Adult	18-60 years	7 or more hours
Older adult	65 years and older	7-8 hours

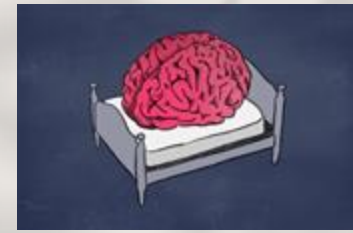
Sleep is critical for healthy brain function



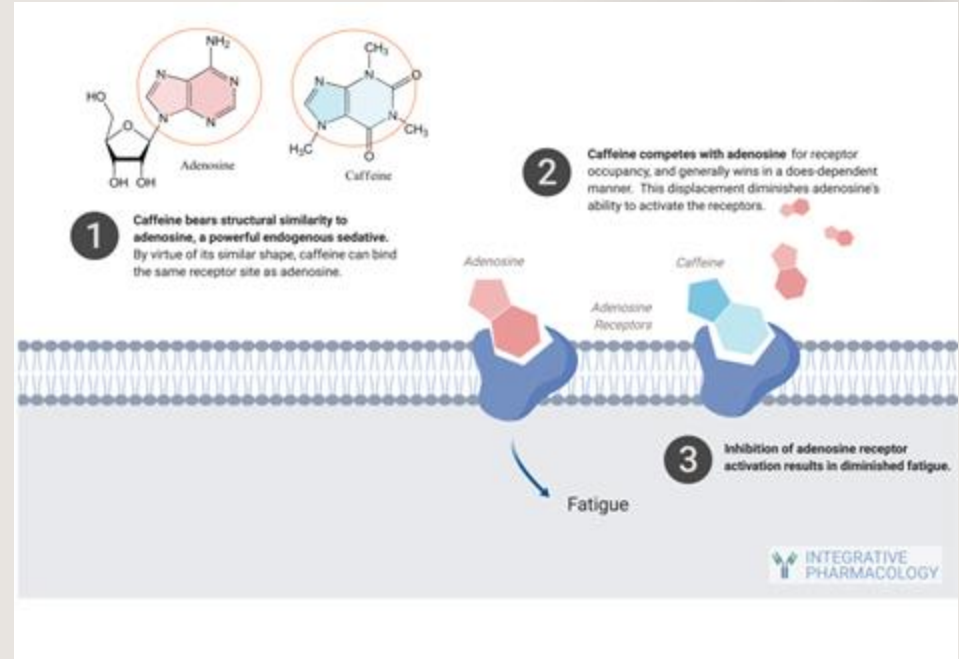
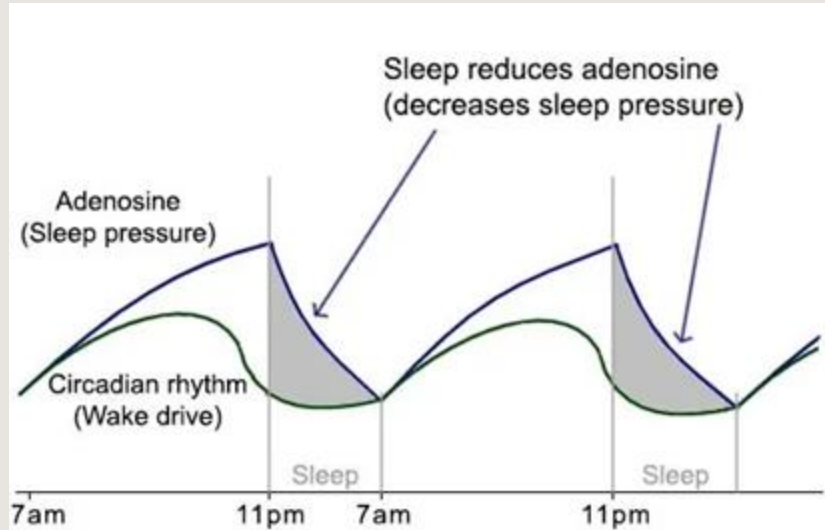
- Why do we need to sleep?
 - Rest / conserve energy?
 - Metabolism decreases only 25%
 - Consolidate memories?
 - Sleep deprivation impairs memory
 - Even a nap enhances some memory
 - Maintain / repair the brain?
 - Proteins are synthesized
 - Myelin is produced / refreshed
 - Clearing waste products



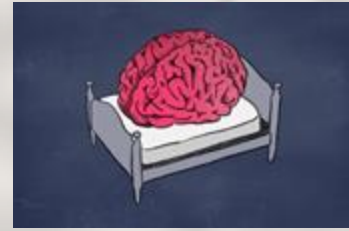
Sleep is critical for healthy brain function



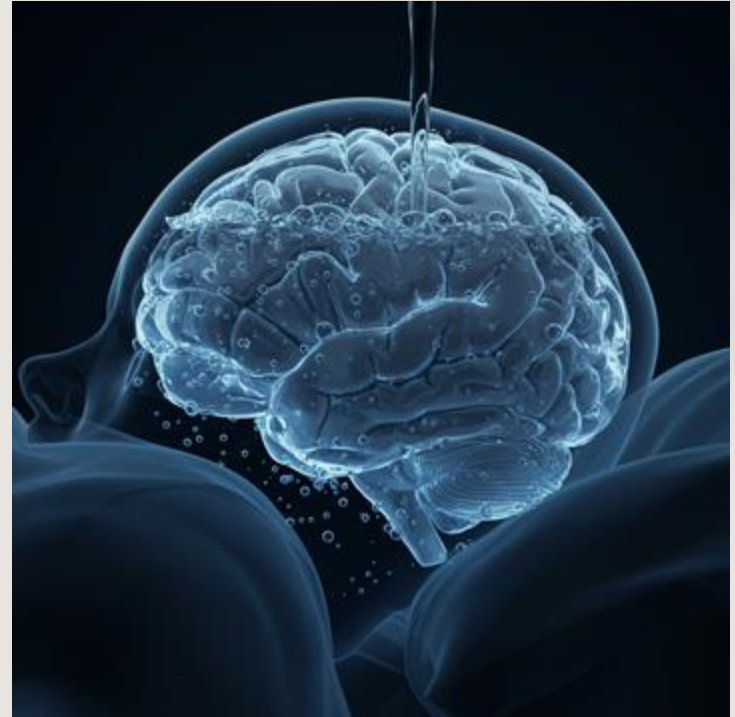
- Adenosine induces sleep (countered by caffeine)



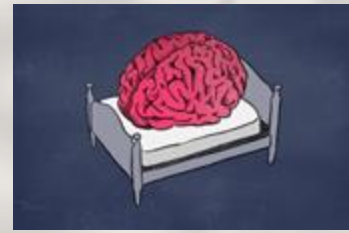
Sleep is critical for healthy brain function



- Glymphatic system
 - Removes waste products
 - Most active in deep sleep (N3)
 - Inadequate / disrupted sleep doesn't allow optimal "cleaning"
 - Being studied: amyloid clearance problems and Alzheimer's Disease



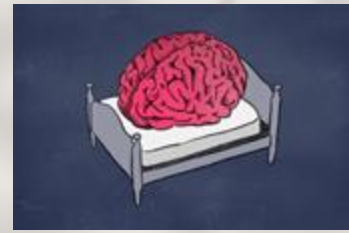
Evidence that PAE impacts sleep



- PAE affects circadian rhythm
expression of core-*CLOCK* genes
 - In children with PAE, *CLOCK* gene expression follows an irregular pattern compared to the typical circadian rhythm
 - In children with PAE, the gene expression levels were lower than typically developing children



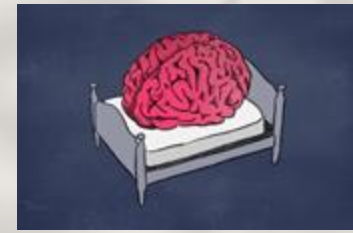
Sleep disruption in FASD



- ~80% of children with FASD have significant sleep problems
 - Insomnia, RLS, circadian disruptions, daytime fatigue
- PAE assoc. with sleep dysfunction
 - Worse quality of sleep
 - Sleep fragmentation
 - Less time asleep
 - Sleep disorders
 - Decreased REM sleep



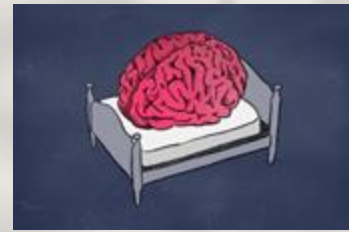
Sleep disruption in FASD



- Breathing-related sleep disorders
 - Apnea / hypopnea
 - Characterized by snoring, stopping breathing, wakings
- Circadian disruption
 - Insomnia (delayed sleep onset)
 - Late sleeping / daytime fatigue
 - Wakings



Disrupted sleep patterns in PAE



- Ex. San Diego State University sleep study
 - 74 participants (35 PAE, 39 Control); Ages 6-10
 - Completed 24-h actigraphy for 2 weeks
 - Sleep diaries & sleep questionnaires
- Findings:
 - Those with PAE were more varied in sleep behaviors than controls
 - PAE participants had more sleep problems as they got older

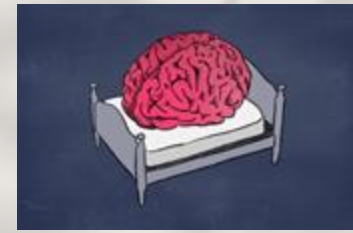


Consequences of sleep disturbances

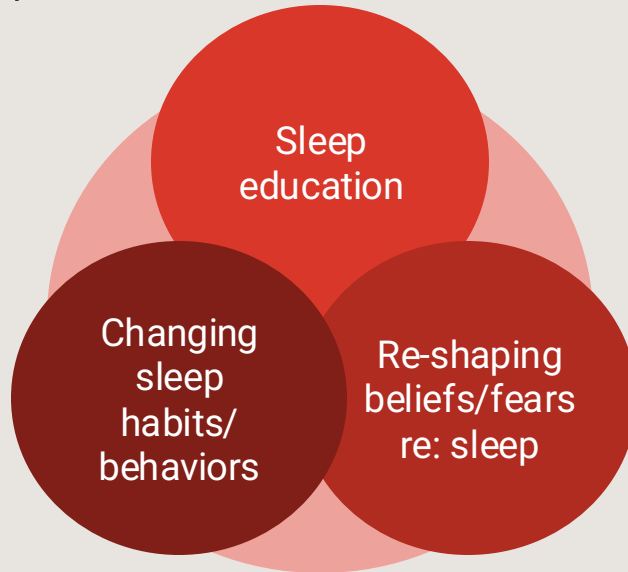
- Daytime fatigue / poor attention
- Hyperactivity / mood dysregulation
- Non-optimized memory performance
- Learning difficulties in school or work



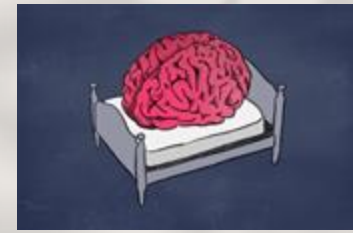
Sleep-based interventions in humans



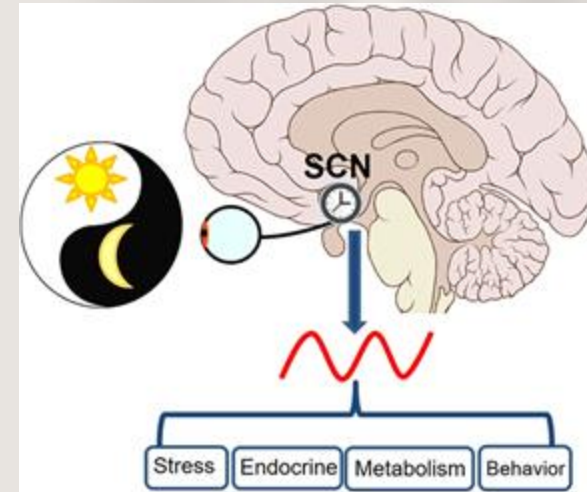
- Cognitive Behavioral Therapy for Insomnia (CBT-I)



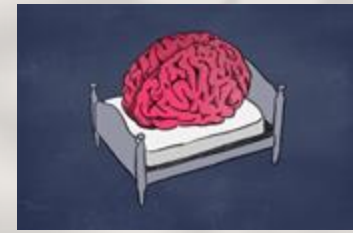
Everyday practical strategies: Sleep



- Understanding circadian rhythms
 - 24-hour clock in the brain (suprachiasmatic nucleus)
 - Many cells fall into rhythm with the SCN
 - Primary inputs that “push” the clock one way or the other
 - Light hitting the eyes
 - Triggers melatonin (natural hormone); level rises and peaks in evening
 - Eating / digestion
 - Exercise / movement



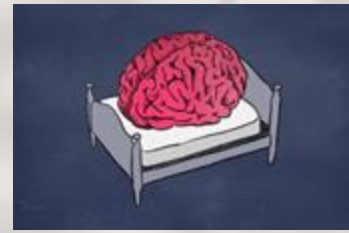
Everyday practical strategies: Sleep



- Sleep hygiene
 - Highly consistent timing
 - Bedtime and wake time
 - Keep routine 7 days per week
 - Consistent bedtime routines
 - Bathing, brushing teeth
 - Lowering lights in the home
 - Pair bed with sleep only
 - No screens/electronics in the bedroom
 - If unable to sleep, move to another room and return when tired



Everyday practical strategies: Sleep



- Sleep hygiene
 - Proper environment
 - Cool temperature
 - Quiet, dark
 - Physiological signals
 - Bright sunlight early in the morning; low light only in evening
 - Healthy meals consistently during the day; no eating in the hours before sleep
 - Exercise regularly in the morning / daytime; avoid aerobic ex. before bed
 - Limit caffeine intake; no coffee or soda after midday
- Melatonin
 - Can help reset circadian rhythm (taken 1 hour before bedtime)
 - Mostly for insomnia; can be counter-productive in other sleep disorders

Exercise and physical activity



Evidence that PAE impacts physical activity



- Voluntary physical activity in rats with PAE improved functioning of hippocampus
 - Cell proliferation
 - Early neuronal maturation
 - Cell survival
 - BDNF expression
 - Synaptic plasticity



Exercise/physical activity-based interventions in humans



- The FAST Club: physical activity intervention for children with FASD to improve executive function
 - Multiple motor activities including games, exercises, and specific skill development
 - Significant improvement on the Children's Color Trails Test (executive function measure)



Exercise/physical activity-based interventions in humans



- Effective interventions in children with various Neurodevelopmental Disorders
 - Attention: Mind-body exercise (i.e. yoga) & Exergaming (i.e. Nintendo Wii Sports)
 - Memory: Exergaming
 - Executive functioning: Exergaming, Mind-body exercise, & Multi-component physical activity (i.e. sports)



Evidence from related conditions



- Children and adolescents with ASD
 - Cognitive and social deficits associated with lower physical activity levels
 - Older kids and girls have higher risk for sedentary behavior



- 12-week physical activity intervention (table tennis) in male children with ASD
 - Improved gross motor skill and executive function
 - Sustained at 12 weeks after intervention



Everyday practical strategies: physical activity



- Be active as a family
 - Walks
 - Games
- Go places for physical activity
 - Public parks
 - Swimming pools
- Provide equipment for activities
 - Balls
 - Jump ropes
 - Tennis Shoes

PHYSICAL FITNESS
Children and teens need regular exercise to promote physical health and mental wellbeing.

Allegro PEDIATRICS

RECOMMENDATION
KIDS AGE 3-5:
3 hours of active play per day
KIDS & TEENS AGE 6-17:
60 minutes of activity per day

ALL ACTIVITIES COUNT
Encourage the activities that your child loves.
Activity can be done all at once or throughout the day.

HEALTH BENEFITS
Aerobic activities strengthen your heart and improve mood.
Strengthening activities build healthy bones and muscles.

AEROBIC ACTIVITIES

STRENGTH EXERCISES

Functional Exercise



- Training to prepare your body for daily tasks
- Examples of functional exercise for kids
 - Tug-of-war
 - Monkey bars
 - Jump rope
 - Musical Chairs

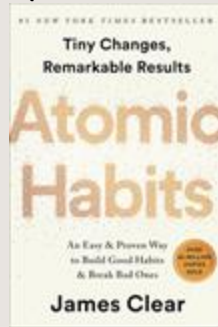


- Physical activity interventions significantly improved cognitive performance
- No significant difference between physical and cognitive interventions effects on cognitive performance

Habit building/stacking



- Attach a new habit to an existing consistent routine
 - Stretch muscles (new habit) before you brush your teeth (current habit) every night



How to:

1. Make a list of current habits
2. Make a list of desired habits
3. Make a “stack” or pairing that works for you
4. Adjust as needed
 - Reduce friction
 - Running shoes near the door
 - Dog or friend to reinforce habit
 - Add reward



Cognitive activity



Evidence that PAE impacts cognitive ability



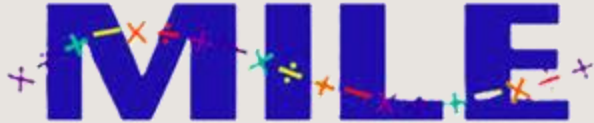
- PAE results in cognitive/behavioral deficits
 - Learning and memory
 - Problem-solving
 - Attention and impulse control
 - Spatial working memory
 - Fine motor
 - Social skill
 - School



Cognitive training interventions for FASD



- Math Interactive Learning Experience (MILE) program conforms caregivers and educators on FASD-specific needs
 - Facilitate math learning and number writing skills
 - Skills for parents/teachers to manage behavioral problems
 - Parent/teacher ratings show improved behavior
 - Significantly improved scores on math measures
- Developed at Emory University by Dr. Coles, Dr. Kable, and Dr. Tadden



- Website: Coles, C. D. *Mile*. Emory University Shield.
<https://med.emory.edu/departments/psychiatry/msacd/research/mile.html>

Cognitive training interventions for FASD



- GoFar program: game-like training
 - Teach self regulation and emotional control
 - Increased focus and reduced impulsiveness
 - Improved attention
 - Disruptive behavior decreased
 - Both FAR and parent-training seem to be required
- Developed at Emory University by Dr. Coles and Dr. Kable
- Website: *Gofar*. Emory University Shield.
<https://med.emory.edu/departments/psychiatry/msacd/research/gofar.html>



Resources: do2learn.com



Cognitive training interventions for FASD



- Similar computer game training programs currently being investigated for their effect on executive functioning
- Small pilot study found music training improved attention in kids with FASD



Cognitive training with neuromodulation: University of Minnesota



- 5-10 sessions of cognitive training
- Time intensive with small effects
- Generalizability challenges
- tDCS assisted cognitive training
 - tDCS can enhance plasticity
 - Combined method has better efficacy and functional outcomes



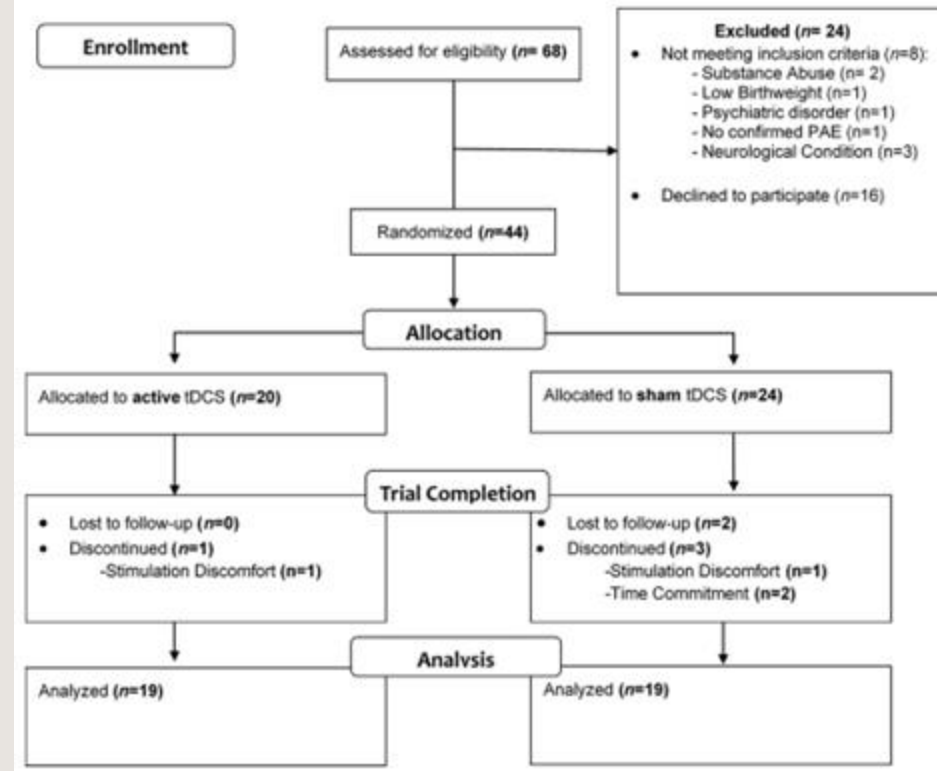
A randomized controlled trial of transcranial direct-current stimulation and cognitive training in children with fetal alcohol spectrum disorder

Elias Boroda^a, Alyssa M. Krueger^a, Priya Bansal^b, Mariah J. Schumacher^a, Abhrajee V. Roy^a, Christopher J. Boys^a, Kelvin O. Lim^a, Jeffrey R. Wozniak^{a,*}

^a University of Minnesota, Twin Cities, USA

^b University of Maryland, USA

- Randomized Controlled Trial from 2017-2020
 - Testing feasibility and efficacy
 - Ages 9 to 16
- Compared active tDCS vs sham tDCS paired with cognitive training

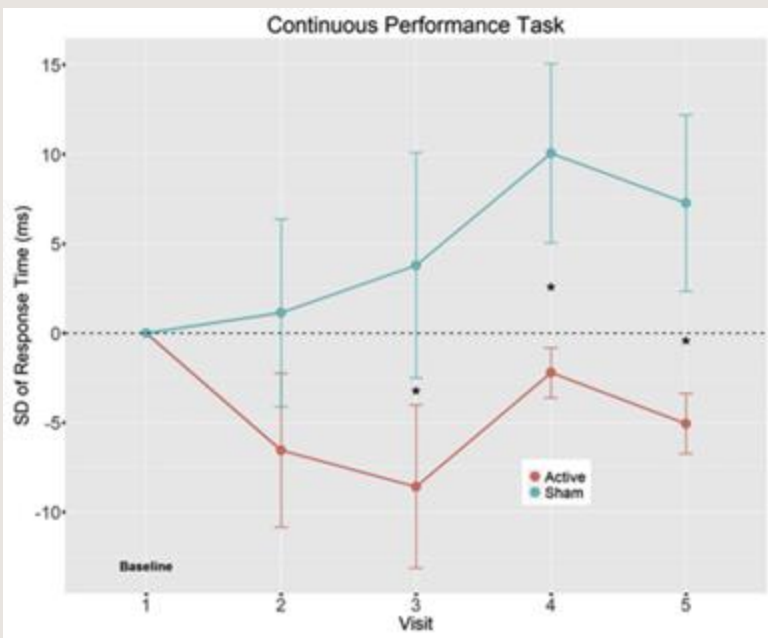


A randomized controlled trial of transcranial direct-current stimulation and cognitive training in children with fetal alcohol spectrum disorder

Elias Boroda ^a, Alyssa M. Krueger ^a, Priya Bansal ^b, Mariah J. Schumacher ^a, Abhrajee V. Roy ^a, Christopher J. Boys ^a, Kelvin O. Lim ^a, Jeffrey R. Wozniak ^{a,*}

^a University of Minnesota, Twin Cities, USA

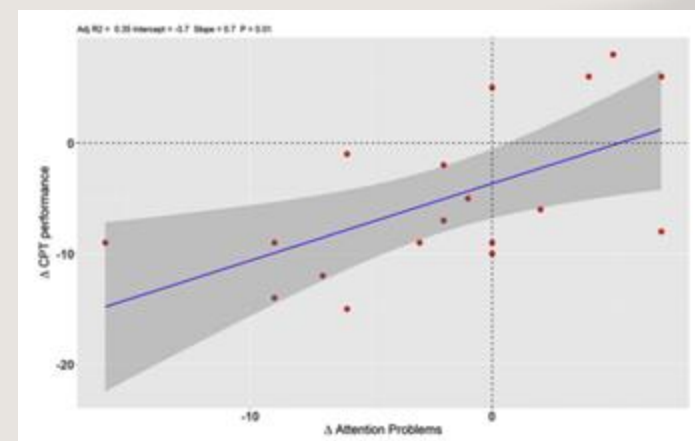
^b University of Maryland, USA



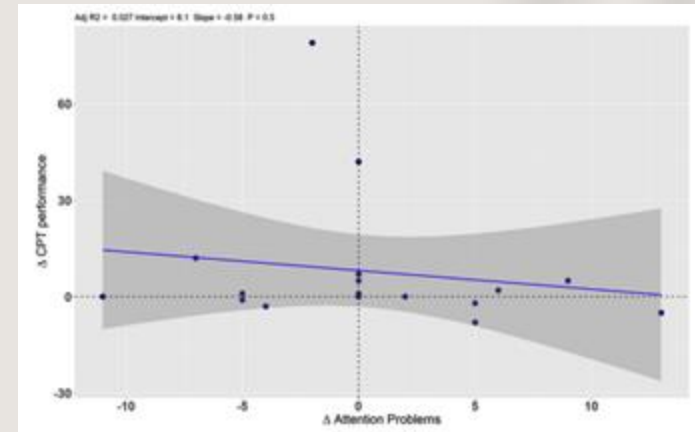
- 86% completed (motivating)
- Small significant improvement of attention for active vs. sham ($p=0.04$)
- No effect on working memory, trail making task, or verbal fluency test



- tDCS was well-tolerated by children & adolescents with FASD
 - No between group differences in side-effects
 - Attention improvements correlated with decrease in ADHD symptoms (parent-report)



Correlation between attention scores and parent-report of active participants



Correlation between attention scores and parent-report of sham participants

<https://doi.org/10.1016/j.brs.2020.04.015>

Evidence from related conditions



- ASD behavioral intervention Early Start Denver Model (ESDM)
 - Based on applied behavior analysis (ABA) methods
 - Behavioral outcomes:
 - Improved cognitive skills measured by Mullen Scales of Early Learning & Vineland Adaptive Behavior Scales
 - EEG outcomes:
 - Increased brain activity related to attention engagement and active cognitive processing of social stimuli



Everyday practical strategies: Cognitive training



- Widely available online cognitive training programs
 - Brain HQ (brainhq.com)
 - Lumosity (lumosity.com)
- Key elements:
 - Repeated practice
 - Varied cognitive activities
 - Sequential / increasing difficulty
 - Motivation to engage focus



Activities that utilize cognitive flexibility and executive function



- Puzzles
 - Spatial skills development
- Reading
 - Working memory, inhibition, fluid intelligence, and cognitive flexibility



Activities that utilize cognitive flexibility and executive function

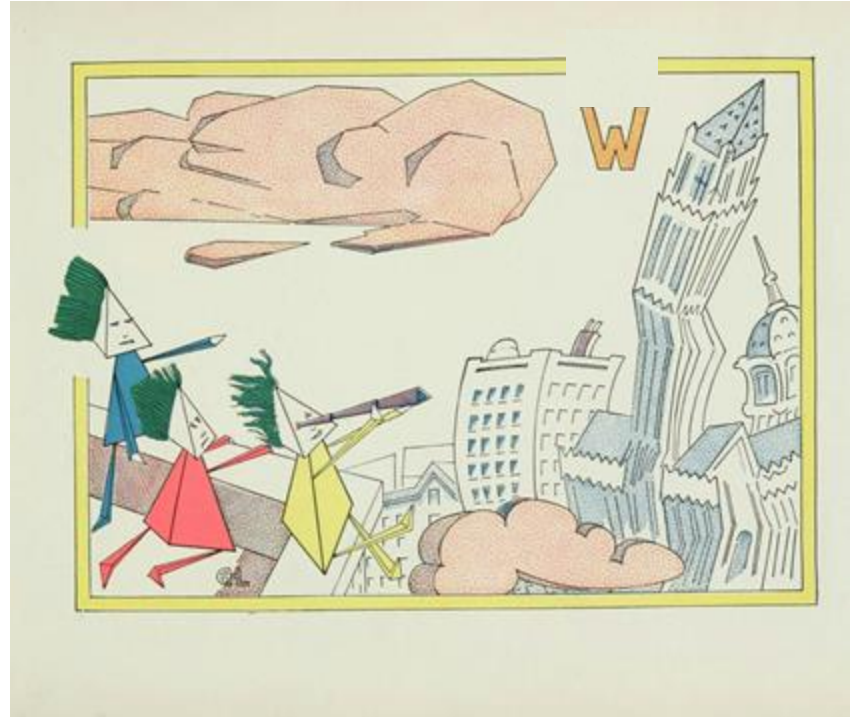


- Music lessons
 - Inhibition, selective attention, and working memory
- Learning a second language
 - Increases the grey matter in the left inferior parietal cortex (IPL)
 - Continues to grow as proficiency increases
 - Left IPL responsible for social cognition and language function



Conclusions

- Research continues to understand how, when, and for whom lifestyle interventions are most effective
- Healthy habits support brain development and health for those with PAE - regardless of FASD-specific diagnosis





UMN FASD research team 2004 to present



