Moving the Needle in Understanding Motor Challenges in Neurodevelopmental Disorders (NDDs)

UCLA Tarjan Center Forum on Neurodevelopmental Disabilities
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UCLA MATTEL Children's Hospital

UCLA CART
CENTER FOR AUTISM RESEARCH AND TREATMENT

Disclosures

Funding: NIH, HRSA, Simons Foundation, Autism Science Foundation, USTA, Best practices committee ACEing Autism

Outline

1. Motor challenges in NDDs, Autism and Genetic Neurodevelopmental Syndromes
2. Measuring motor function as biomarkers to predict developmental concerns
3. Comprehensive motor measurement in genetic neurodevelopmental syndromes
4. Organized physical activity (OPA) as an intervention for motor challenges in Neurodevelopmental Disorders

Importance of motor function

Motor development is the earliest benchmark of developmental progress and is crucial in driving multiple cognitive processes

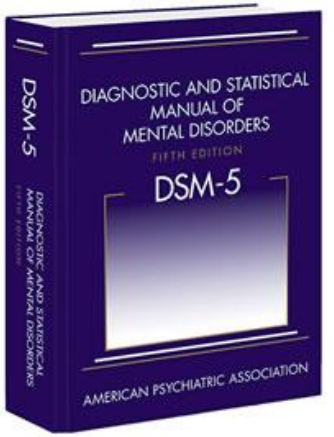
Motor impairments are prevalent and one of the first signs of atypical development in ASD and many Neurodevelopmental Disorders (NDDs)

Motor development can be observed and measured over time

Motor function can serve as a target for intervention

(Bhat et al, 2011; Fournier et al, 2010 ; Wilson RB et al, 2018; Piven, 2018; Iverson et al, 2019; Ozonoff et al, 2011)

Motor abnormalities are prevalent in NDDs



Autism Spectrum Disorder: “associated deficit, such as odd gait, clumsiness, and other abnormal motor signs”

Attention-Deficit/Hyperactivity Disorder: “delays in motor often occur”

Intellectual Disability: “delayed motor, language, and social milestones may be identifiable in the first 2 years of life”

(Fournier et al, J Autism Dev Disord, 2010; Wilson et al, Aus Res 2020)

DSM-5 Diagnostic Criteria for ASD

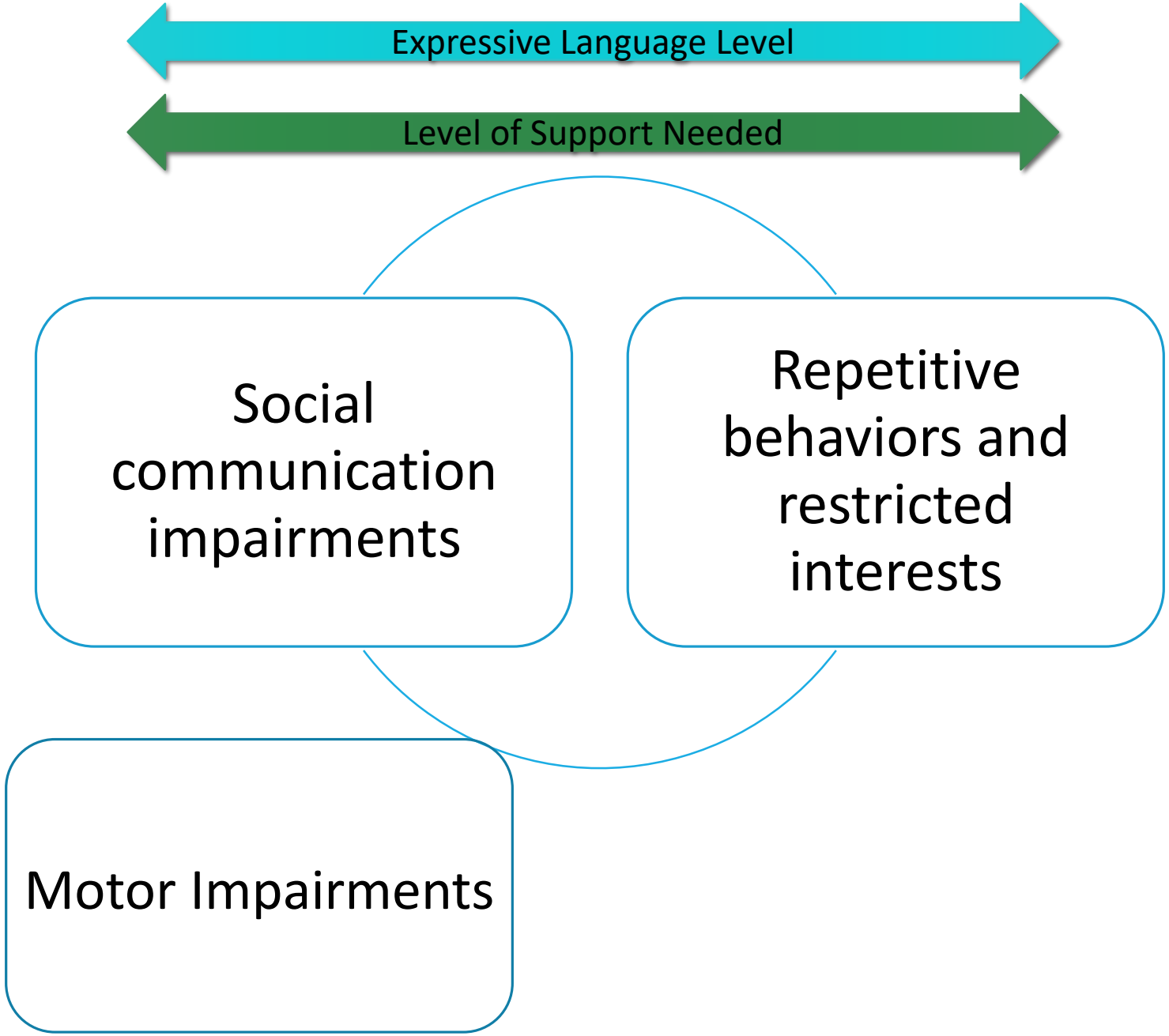
1. Deficits in social-emotional reciprocity
2. Deficits in nonverbal communicative behaviors used for social interaction
3. Deficits in developing, maintaining and understanding relationships

Need symptoms in all 3 subdomains

1. Stereotyped or repetitive motor movements, use of objects or speech
2. Insistence on sameness, inflexible adherence to routines
3. Highly restricted, fixated interests that are abnormal in intensity or focus
4. Hyper- or hyporeactivity to sensory input or unusual interest in sensory aspects of the environment

Need symptoms in 2 of 4 subdomains

1. Odd Gait
2. Clumsiness
3. Other abnormal motor signs



Prevalence of Motor Difficulties in Autism Spectrum Disorder: Analysis of a Population-Based Cohort

Melissa K. Licari, Gail A. Alvares, Kandice Varcin, Kiah L. Evans, Dominique Cleary, Siobhan L. Reid, Emma J. Glasson, Keely Bebbington, Jess E. Reynolds, John Wray, and Andrew J. O. Whitehouse

- 2,084 individuals with ASD
- **35.4%** met criteria for motor impairments (rate almost as common as intellectual disability-37%)
- Prevalence of motor difficulties increased with age
- Diagnosing clinicians reported motor difficulties in only **1.34%** of cases

(Licari et al., *Autism Research* 2020)

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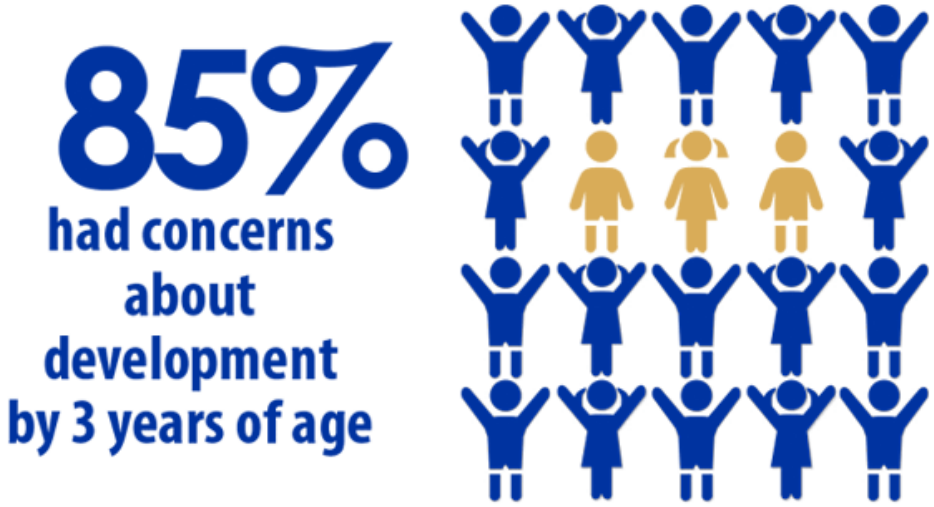
Delays in Autism Early Identification

1 in 36 children with ASD diagnosis

Average age of diagnosis remains at 4 years

Symptoms emerge earlier, even in the first year of life



https://www.cdc.gov/

Addressing these issues

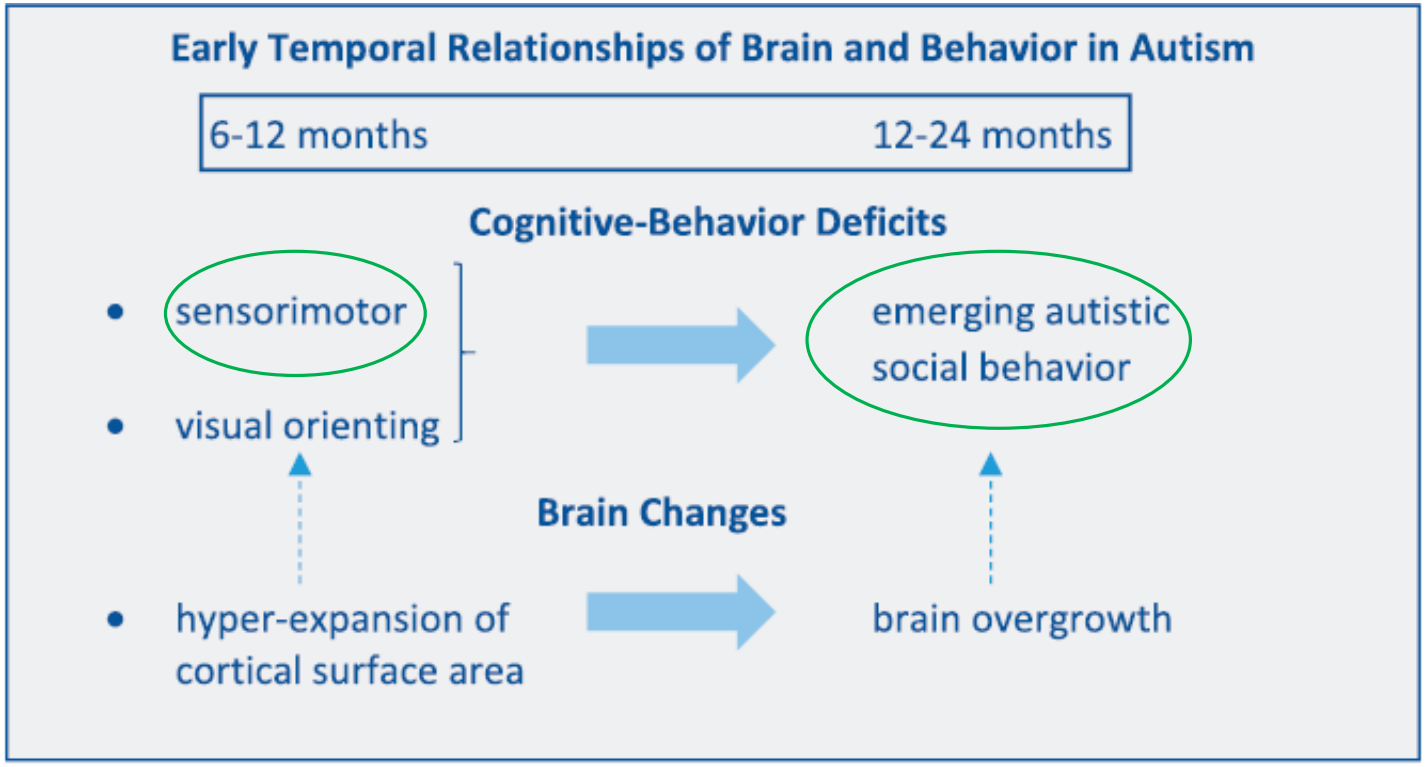
Increase our training efforts and clinical workforce

Identify markers of risks and challenges that can be objectively and reliably measured

Infants with familial risk for ASD

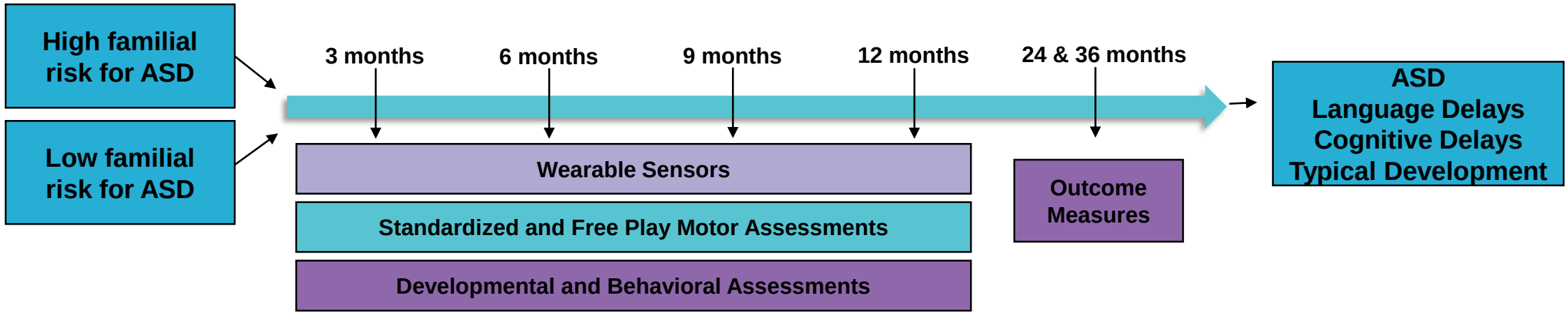
An older sibling with ASD raises risk of ASD diagnosis by **20%** and other delays by **35%**

Motor abnormalities are one of the first signs of atypical development



(Ozonoff et al., 2011; Charman et al., 2017; Piven et al, 2017)

Motor impairments as predictive biomarkers



Develop quantitative, objective, and scalable motor biomarkers
Monitor change and stability of the biomarker
Evaluate predictive ability of motor biomarkers

sensors

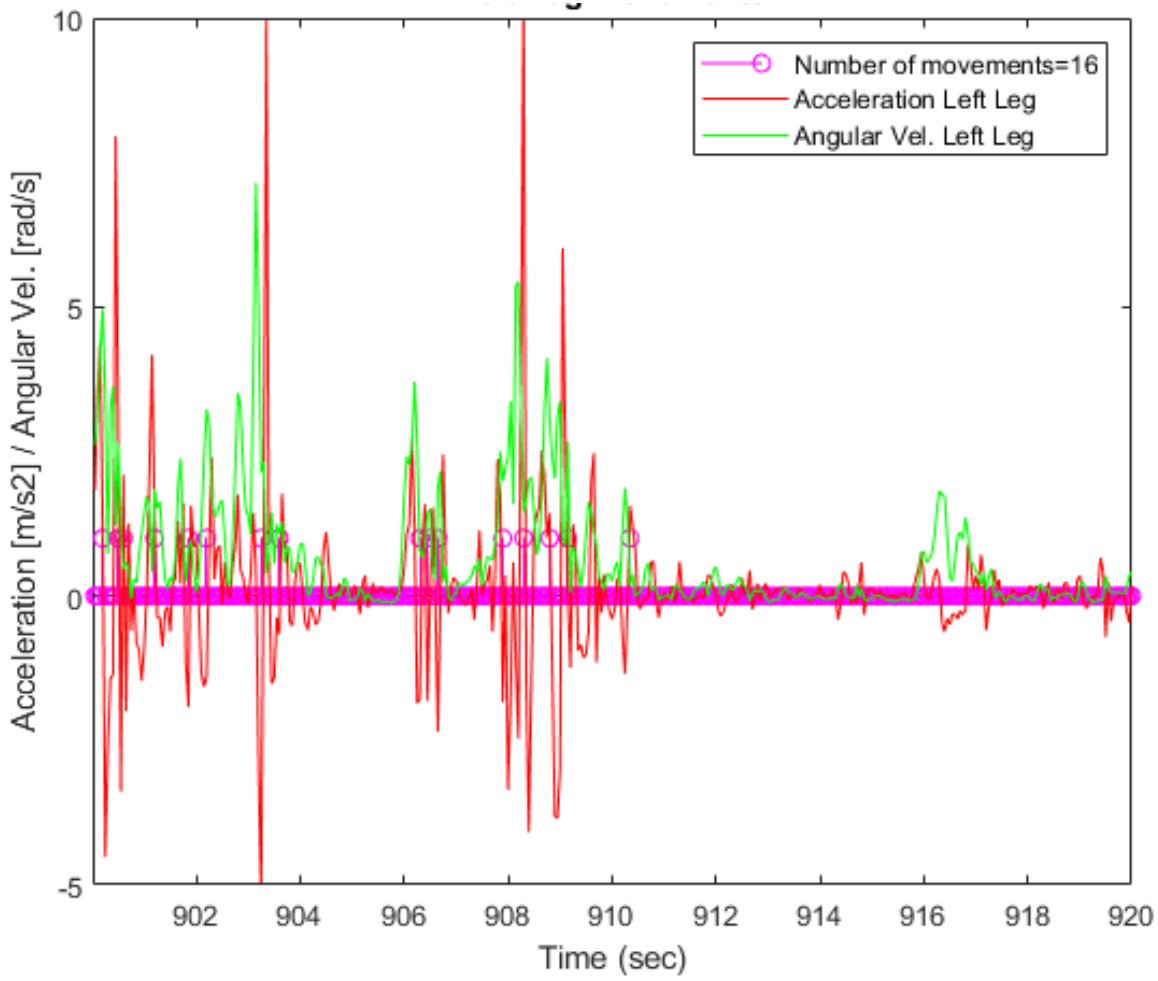
Article

Using Wearable Sensor Technology to Measure Motion Complexity in Infants at High Familial Risk for Autism Spectrum Disorder

CNS 2023
CHILD NEUROLOGY SOCIETY
52nd ANNUAL MEETING

- Single infant movements are extracted from the data using a validated algorithm

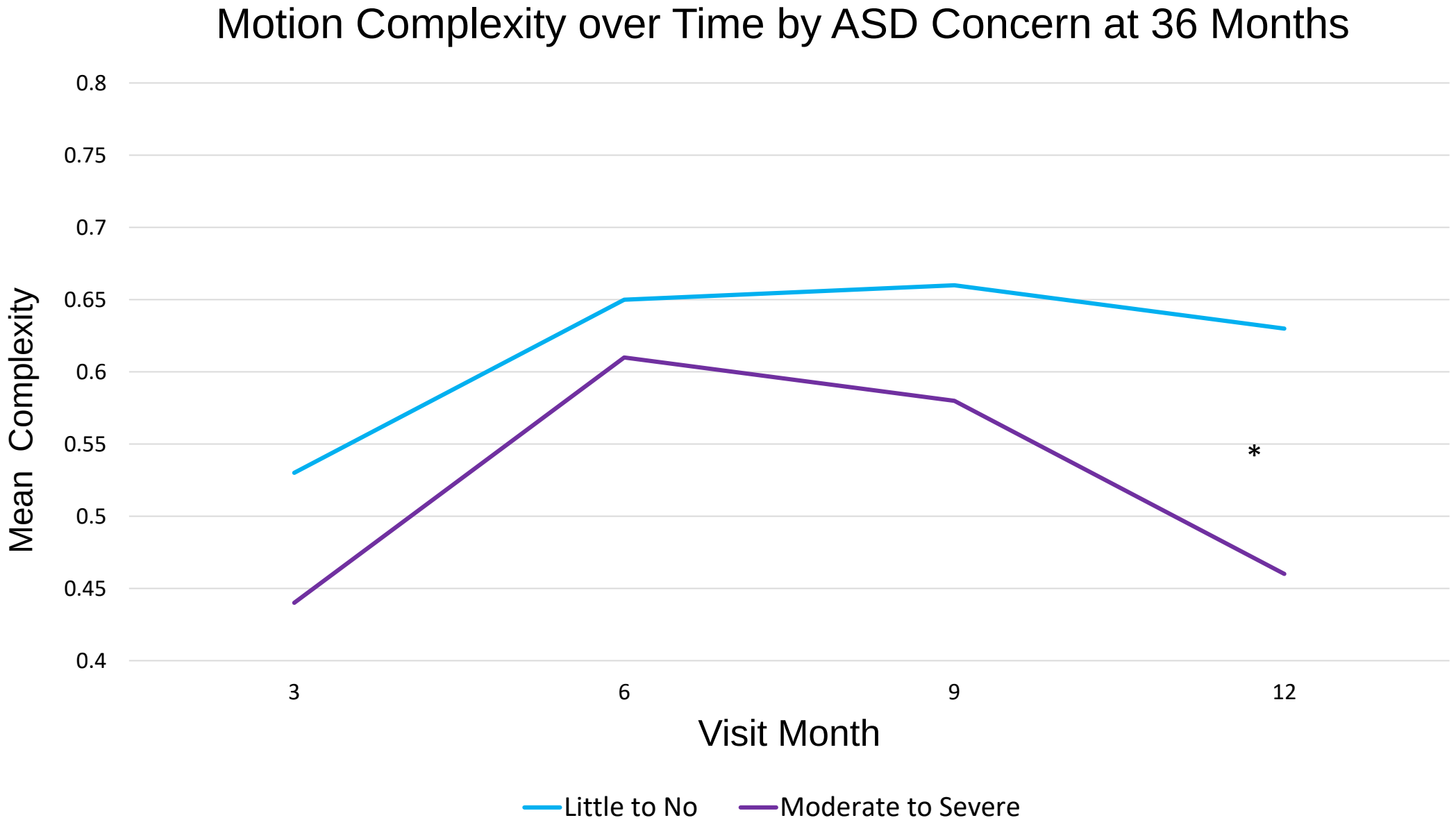
- Create of novel movement measures from the data such as complexity



(Smith, BA, et al, 2015, Wilson, RB, et al, 2021)

Qualitatively what does this mean…

- Complex repertoire of movements are important for healthy, non-repetitive motor development
- Infants may not be producing the same quality or repertoire of spontaneous movements
- This lack of a full repertoire/optimal complexity underlies later motor delays
- Also impacts other areas of behavioral and cognitive development


Motion Complexity over Time by ASD Concern at 36 Months
Mean Complexity
0.8
0.75
0.7
0.65
0.6
0.55
0.5
0.45
0.4
3
6
9
12
Visit Month
*
Little to No
Moderate to Severe

N = 25 infants

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Genetic Neurodevelopmental Syndromes

Dup15q Alliance

FOR 15Q 11.2–13.1 MULTIPLICATIONS

Quantitative Gait Analysis in Duplication 15q Syndrome and Nonsyndromic ASD.

Apr 13, 2020 | Published Research

ARRE

ASXL RARE RESEARCH ENDOWMENT

Newsletter

Update from gait and movement study at UCLA

Identification of Developmental and Behavioral Markers Associated With Genetic Abnormalities in Autism Spectrum Disorder

Somer L. Bishop, Ph.D., Cristan Farmer, Ph.D., Vanessa Bal, Ph.D., Elise B. Robinson, Ph.D., A. Jeremy Willsey, Ph.D., Donna M. Werling, Ph.D., Karoline Alexandra Havdahl, Ph.D., Stephan J. Sanders, M.D., Ph.D., Audrey Thurm, Ph.D.

Identification of a distinct developmental and behavioral profile in children with Dup15q syndrome

Charlotte DiStefano[1*], Amanda Gulsrud[1], Scott Huberty[1], Connie Kasari[2], Edwin Cook[3], Lawrence T. Reiter[4], Ronald Thibert[5] and Shafali Spurling Jeste[6]

What's missing in autism spectrum disorder motor assessments?

Rujuta B. Wilson[1*], James T. McCracken[1], Nicole J. Rinehart[2] and Shafali S. Jeste[1]

- Higher rates and earlier presentation of motor challenges
- Challenges are uniquely associated with language and communication

What's missing in autism spectrum disorder motor assessments?

Rujuta B. Wilson[1*], James T. McCracken[1], Nicole J. Rinehart[2] and Shafali S. Jeste[1]

Lack of motor assessments that can be used to assess individuals with varying cognitive and behavioral function

Motor assessments in individuals with ID often have a "floor effect"

Move beyond capturing only motor milestones and skill acquisition

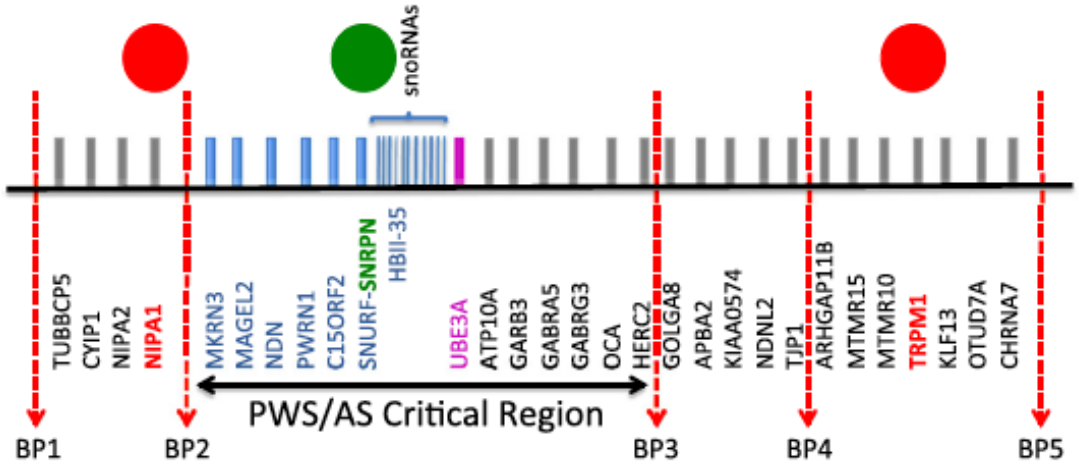
Precisely measure qualitative differences in motor function

(Wilson RB et al, JNDD 2018)

MABC-2 Gait and balance

Dup15q syndrome

Maternally derived duplications of 15q11.2-q13.1 region are one of the most frequently reported copy number variant in ASD (3-5% of ASD)



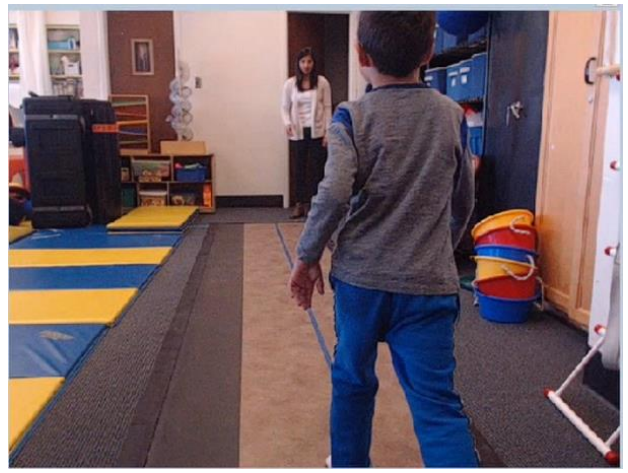
Hypotonia and motor delays (90%)
Global developmental delay (80%)
Autism Spectrum Disorder (50-80%)
Epilepsy (50%)

(Al Ageeli, 2014; Urraca, 2013; Hogart, 2010; Battaglia, 2010; Conant, 2014; Finucane, 2016)

RESEARCH ARTICLE

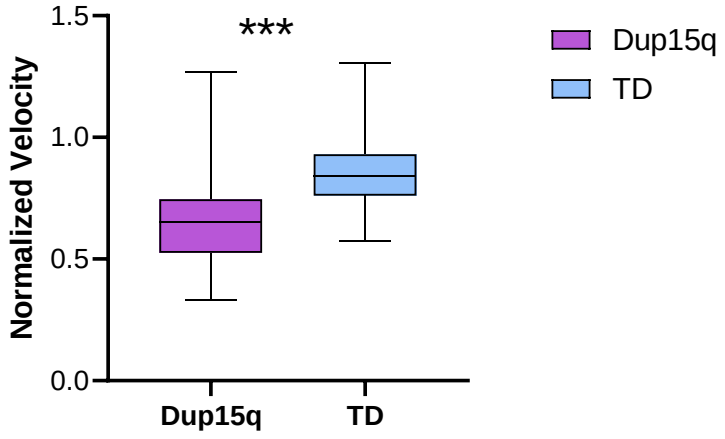
Quantitative Gait Analysis in Duplication 15q Syndrome and Nonsyndromic ASD

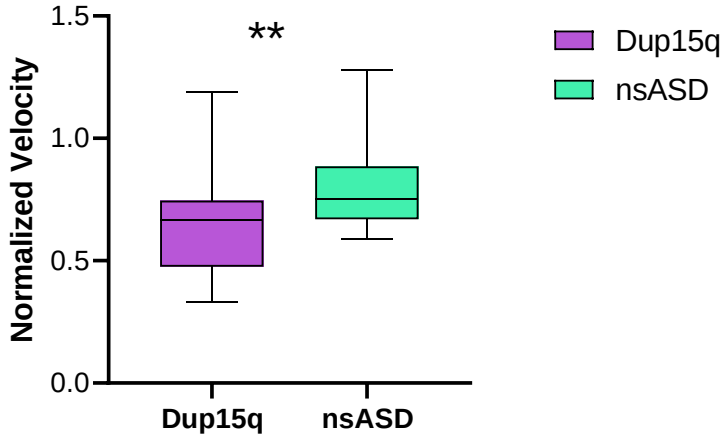
Rujuta B. Wilson, David Elashoff, Arnaud Gouelle, Beth A. Smith, Andrew M. Wilson, Abigail Dickinson, Tabitha Safari, Carly Hyde, and Shafali S. Jeste

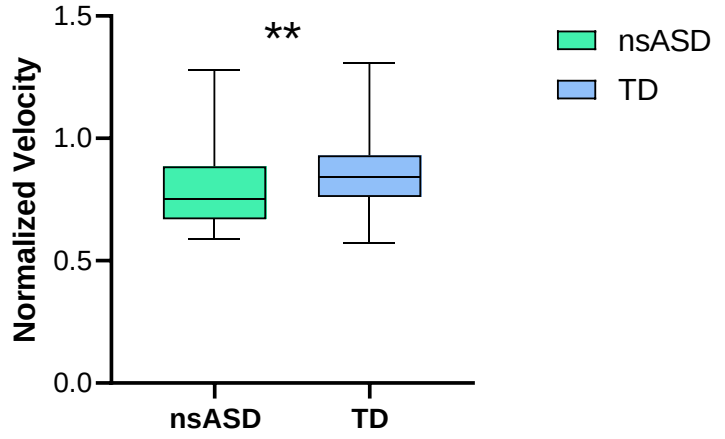


Three domains of gait: pace, postural control, variability

Dup15q (n = 39), Non-syndromic (ns) ASD (n = 21), and TD (n = 131)







"The ultimate goal of this work is to develop quantitative motor parameters that could serve as translational clinical endpoints for future treatment trials in this syndrome."

Examining the neurodevelopmental and motor phenotypes of ASXL Conditions

Chromatin Modifying Disorders (CMDs) are one of the most rapidly expanding disorders associated with ASD and Intellectual Disability

Present with a range of motor impairments

Multi-modal motor assessment: parent questionnaires, quantitative analysis, direct examination

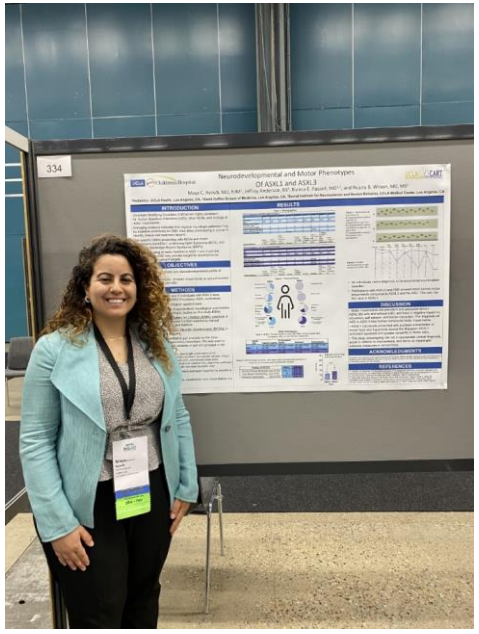
Examining the neurodevelopmental and motor phenotypes of ASXL Conditions

Multi-modal motor assessment: parent questionnaires, quantitative analysis, direct examination

ASXL 1: mixed hypo and hypertonia, slower gait, poorer postural control

ASXL 3: ASD diagnosis associated with greater motor impairments

Motor difficulties negatively impacted school activities, self-esteem, and social interactions



Maya Ayoub, MD, EdM,
Child Neurology Resident, PGY5

(Ayoub et al., revisions pending)

CHAMPION

Chromatinopathies and Autism: Motor Phenotyping and Indicators of Neurodevelopment

SFARI SIMONS FOUNDATION AUTISM RESEARCH INITIATIVE

UCLA Researchers are doing a study to learn about motor, cognitive, and behavioral developmental in children with ADNP that are 1-5 years of age. The study has options for an in person visit at UCLA or a virtual study visit.

Verbal and written feedback about child's development and $100 compensation

If you are interested in having your child participate in this study or would like to seek additional information, you can contact the study coordinator via email or phone: RQLy@mednet.ucla.edu / 310-206-1045.

http://wilsonmotorlab.org/champion/

Summary and Next Steps

- Motor challenges are prevalent and pervasive in NDDs and genetic neurodevelopmental syndromes.
- Quantitative tools can improve characterization of motor impairments
- Complexity and variability may provide insight on predictive motor biomarkers

- Expanding these metrics in the community

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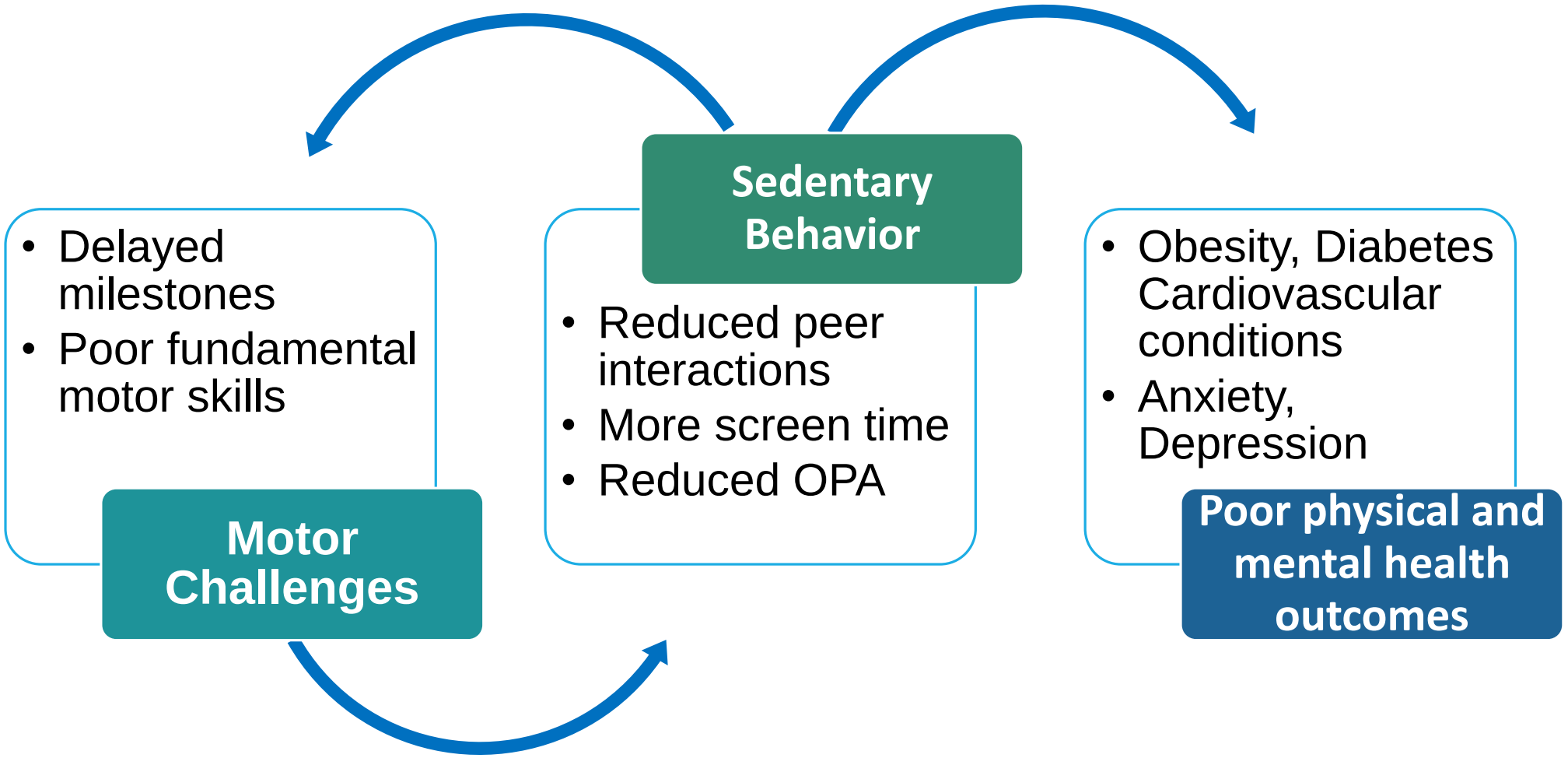
Impacts on Physical Health and Wellbeing



(Roetart P., 2015; Srinivasan et al, 2014; Jones et al 2016; Gehricke et al., 2020)

Benefits of organized physical activity (OPA)

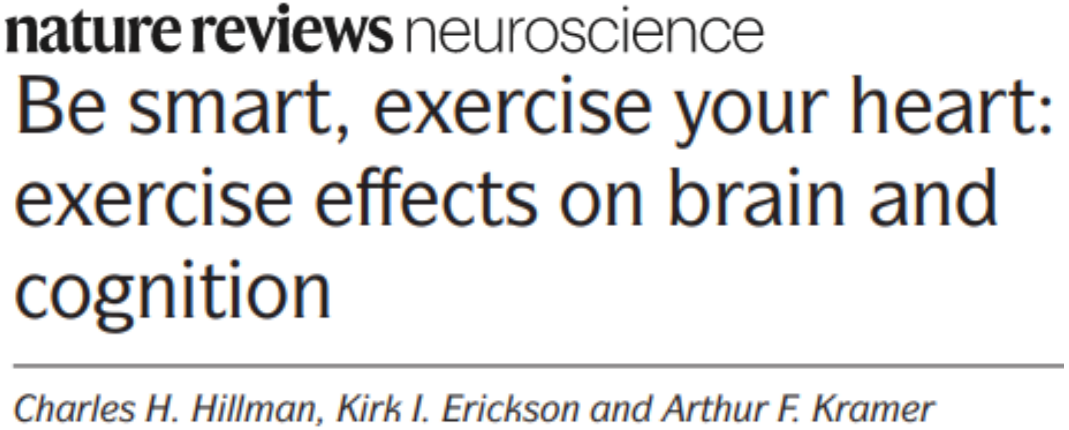
Good for the Brain

Long term health benefits

Mental Health Benefits

Cognitive benefits

Building social relationships



“As fitness has also been related to the frontoparietal network, it would follow that children might derive benefits in school performance from increased participation in physical activity”.

(Chekroud SR, et al., Lancet Psych 2018; Ishihara & Mizuno, Eur J Sport Sci, 2018)

Benefits of OPA for children with autism

Organized physical activity programs: improving motor and non-motor symptoms in neurodevelopmental disorders

Nicole J. Rinehart, Shafali Jeste, Rujuta B. Wilson
Dev Med Child Neurol 2018

A Meta-Analytic Review of the Efficacy of Physical Exercise Interventions on Cognition in Individuals with Autism Spectrum Disorder and ADHD

(Tan et al., J Autism and Dev Disord, 2016)

Outcomes of OPA for individuals with NDDs

48-week program focused on basic coordination and strength exercises vs control

Children with ASD (6-12 y/o)

→ Improved lipid profile, perceived quality of life, and repetitive and stereotyped behaviors

(Toscano et al., Percept Mot Skills, 2018)

12-week remote exercise intervention

1 vs 2 x per week

Adults with Down Syndrome (18-35 y/o)

→ 2 x per week led to significant improvement in memory and nonsignificant in attention and reaction time

(Ptomey et al., Disabil Health J, 2018)

10-week swimming intervention vs control

Children with ASD (6-9 y/o)

→ Improved social competence

Reduced irritability

(Pan CY, Autism, 2010)

Emily Coker,
Founder, EMI

EMI
expressive movement initiative

Mission

Provide an expressive outlet for children with disabilities

Foster mentorship and a sense of community among students and volunteers

Eliminate the stigma and reduce the challenges associated with disability on the UCLA campus and beyond

Dance club seeks to provide inclusive, accessible space for kids with disabilities

- Founded at UCLA in 2019
- UCLA Student Run Organization-50 volunteers
- Training in NDDs, disparities in care, benefits of OPA, adapting movement skills
- Served over 150 children in person and over 60 children virtually (nationally)

EMI
expressive movement initiative

https://www.emiucla.org/

Improving Awareness, Identification, and Treatment of Motor Impairments in Autism

PEDIATRICS®

Rujuta B. Wilson, MD, MS

Autism Intervention Research Network on Physical Health

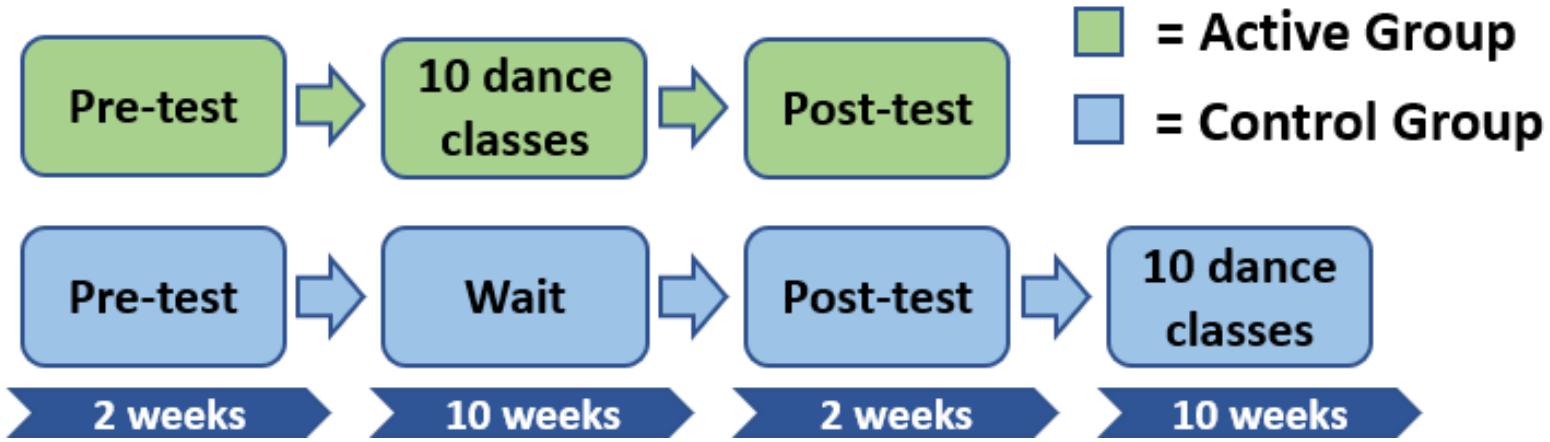
Neurology Node Core Project:

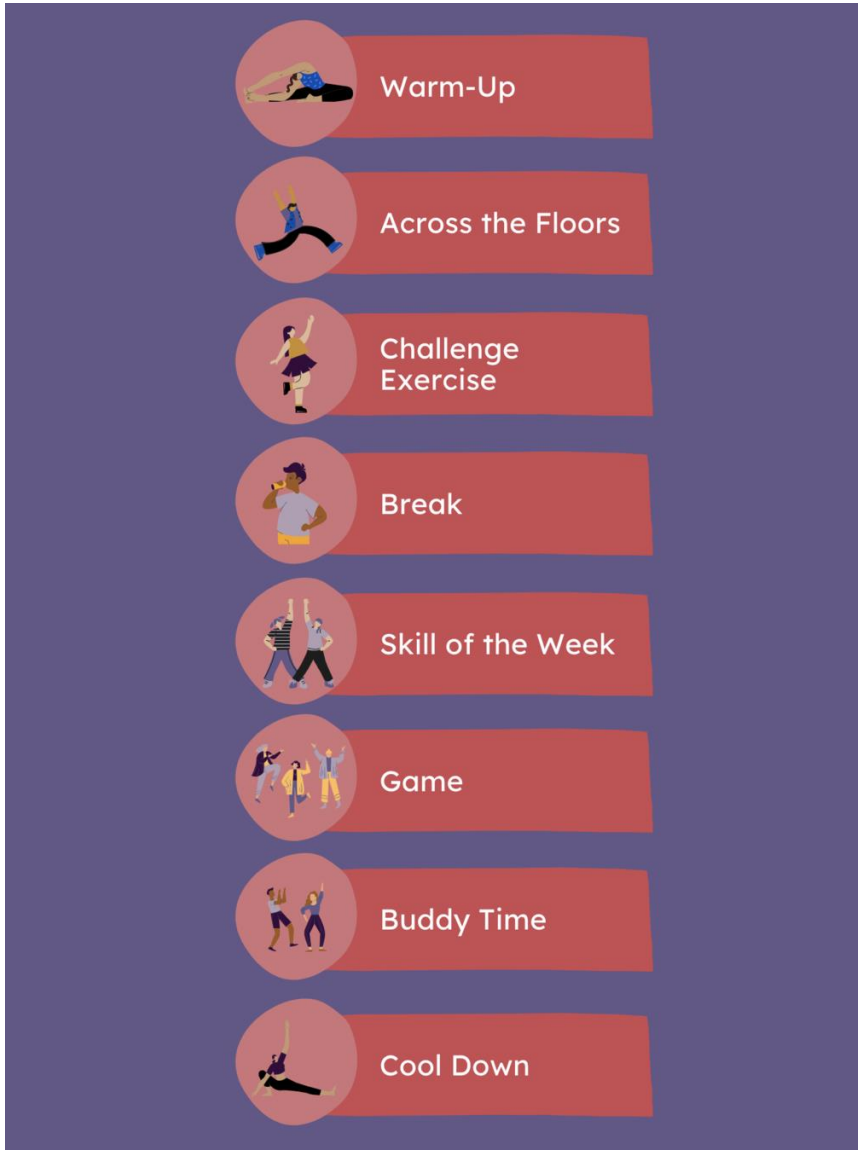
“There is a need for evidence based OPA for autistic individuals. However, there remains a paucity in the literature regarding evidence based OPA for autistic individuals and the outcomes associated with these programs.”

EMI Intervention Clinical Trial

Study Design

- Randomized waitlist-controlled trial

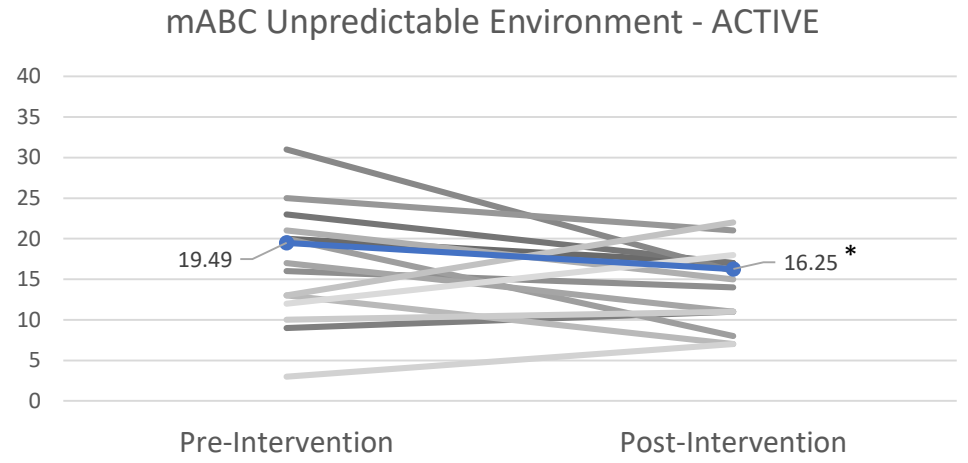


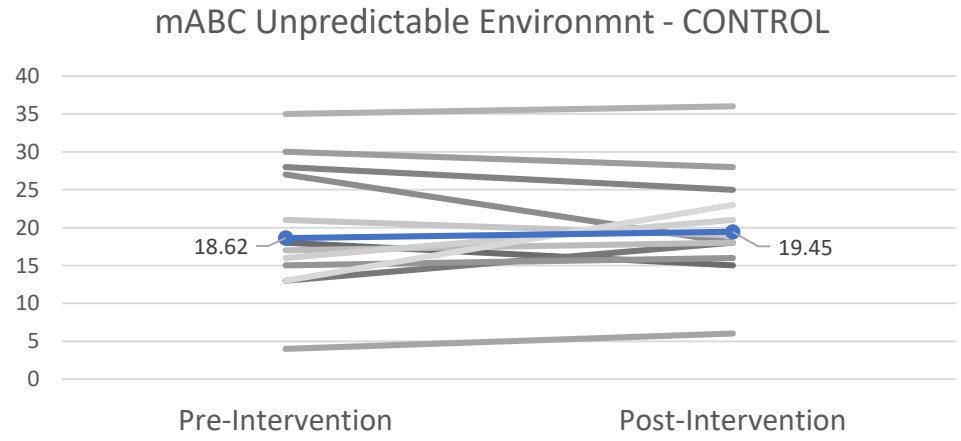


Expressive Movement Initiative Intervention Pilot Study

Measures

- Significant improvement in motor skills in a dynamic environment
- Improvement in social communication skills measured on the SRS





(Anderson JT, et al., 2023, submitted)

Clinical Tips and Referral to OPA

Routine screening for motor challenges in individuals with NDDs

- Developmental history, DCDQ
- Referral to programs adapted for children with autism
- Recommend activities for families that reduce sedentary behaviors

Help the family create a medical profile for the child (e.g., information on seizures, behavioral difficulties, language level)


Welcome to the...
EMI
SKILL
SHOWCASE

Acknowledgements

Thank you for your time and to all the families who participate in our research

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HRSA Health Resources & Services Administration
AIRP
Wilson Motor Lab