

# **AGGRESSION AND SELF-INJURY: RESEARCH NEEDS FOR THE SEVERELY AFFECTED END OF THE SPECTRUM**

**Matthew Siegel, M.D.**

**Associate Professor of Psychiatry & Pediatrics  
Tufts University School of Medicine**

**VPMA, Developmental Disorders Service  
Maine Behavioral Healthcare**

**Faculty Scientist II  
Maine Medical Center Research Institute**

# DISCLOSURES

| Source                                         | Clinical Advisor | Employee | Research Funding |
|------------------------------------------------|------------------|----------|------------------|
| Maine Behavioral Healthcare                    |                  | X        |                  |
| NIMH, Simons Foundation, NLM Family Foundation |                  |          | X                |
| Camp Alsing                                    | X                |          |                  |

# AGENDA

- Aggression and self injury – prevalence and impacts
- Multi-disciplinary approaches to serious challenging behaviors
- Studying the severely affected: The Autism Inpatient Collection (AIC)
- Novel approach to challenging behaviors
- Critical areas for further research

# AGGRESSION AND SELF INJURY: A BIG PROBLEM

**“My son is 19. Severely autistic. Can’t speak. Getting more and more aggressive !!! Not only bites his wrist, he bangs walls and breaks things, and then comes after us. I can’t keep locking myself in a room because he will bang the door down... No doctor in our area knows anything of what to do...Please, please I’m reaching out. There must be something for him...not fair for me and most certainly not fair to him! Cry for help!”**

# AGGRESSION PREVALENCE & IMPACTS

- Up to 2/3 of youth with ASD develop aggression

- Kanne SM, Mazurek MO. *J Autism Dev Disord.* 2011

- Aggression is one of the primary reasons youth with ASD use behavioral healthcare services

- Arnold LE, Vitiello B, McDougle C, et al. *J Am Acad Child Adolesc Psychiatry.* 2003

- Families report that aggression is **often of greater concern and negative impact than the core social and communicative deficits that define ASD**

- Hodgetts S, et al. *Focus Autism Other Dev Disabl.* 2013  
- Farmer CA, Aman MG. *Res Autism Spectr Disord.* 2011

- Studies in ASD suggest that broadly-defined problem behaviors are heightened in ASD compared to typically developing (TD) and intellectually disabled (ID) samples; further, some ASD subgroups engage in persistent or increasing problem behaviors into adulthood.

- Gray K, et al. *Am J Intellect Dev Disabil.* 2012  
- Woodman AC, et al., *Dev Psychopathol.* 2016

# PARTICULARLY FOR THE MINIMALLY VERBAL

- Inability to efficiently report distress makes aggression seem to occur “out of the blue.”
  - Results in:
    - Caregivers unable to anticipate an aggressive outburst
    - Increasingly restrictive educational settings or exclusion
    - Inability to access community
    - High utilization of psychotropics, hospitalizations, out of home placements
    - Limits opportunities for real-time prevention (calming strategies, de-escalation techniques, functional communication)
- The unmeasured effect of serious problem behaviors is a bending of the developmental trajectory downward

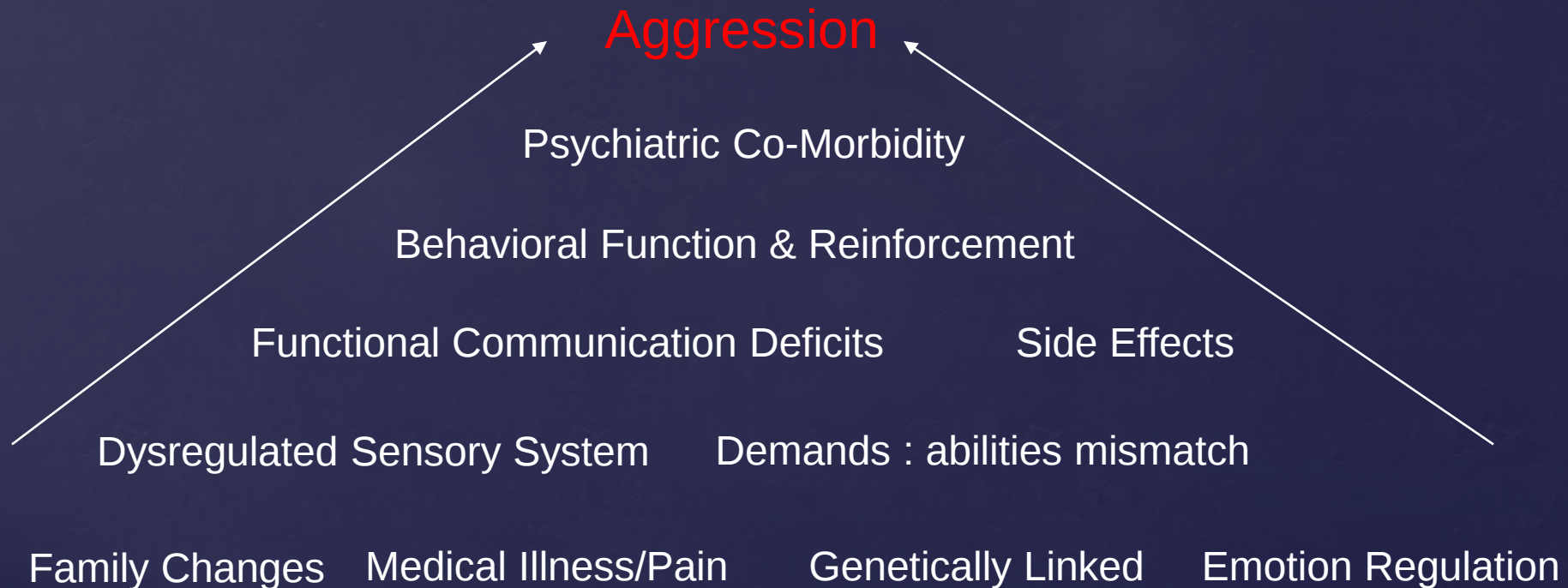
# DEVELOPMENTAL DISORDERS SERVICE

## MAINE BEHAVIORAL HEALTHCARE

Spring Harbor Hospital DD Unit,  
Spring Harbor Academy, Day Treatment,  
Outpatient Clinic, Autism Research Team



# Aggression is A Final Common Pathway Symptom



# FOUNDATION OF TREATMENT

- Highly individualized behavioral plan with embedded communication and occupational therapy supports
- Targeted psychopharmacology
- Transfer of management skills to parents, local school, in-home staff

# MULTI-DISCIPLINARY TREATMENT TEAM

- Child Psychiatry and Pediatrics
- Behavioral Psychologist
- Behavioral Coordinator (BCBA)
- Special Education
- Speech Pathologist
- Occupational Therapist
- Nursing
- Social Work
- Milieu Coordinator (OT)



# THERAPEUTIC APPROACHES FOR CHALLENGING BEHAVIORS

- Applied Behavioral Analysis
- Psychotropic Medication

30% of functional behavioral assessment studies are inconclusive about behavioral function

- Derby KM, et al, 1992, *J Appl Behav A*; Iwata BA, et al., *J Appl Behav Anal.* 1994; Vollmer TR, et al., *J Appl Behav Anal.* 1994

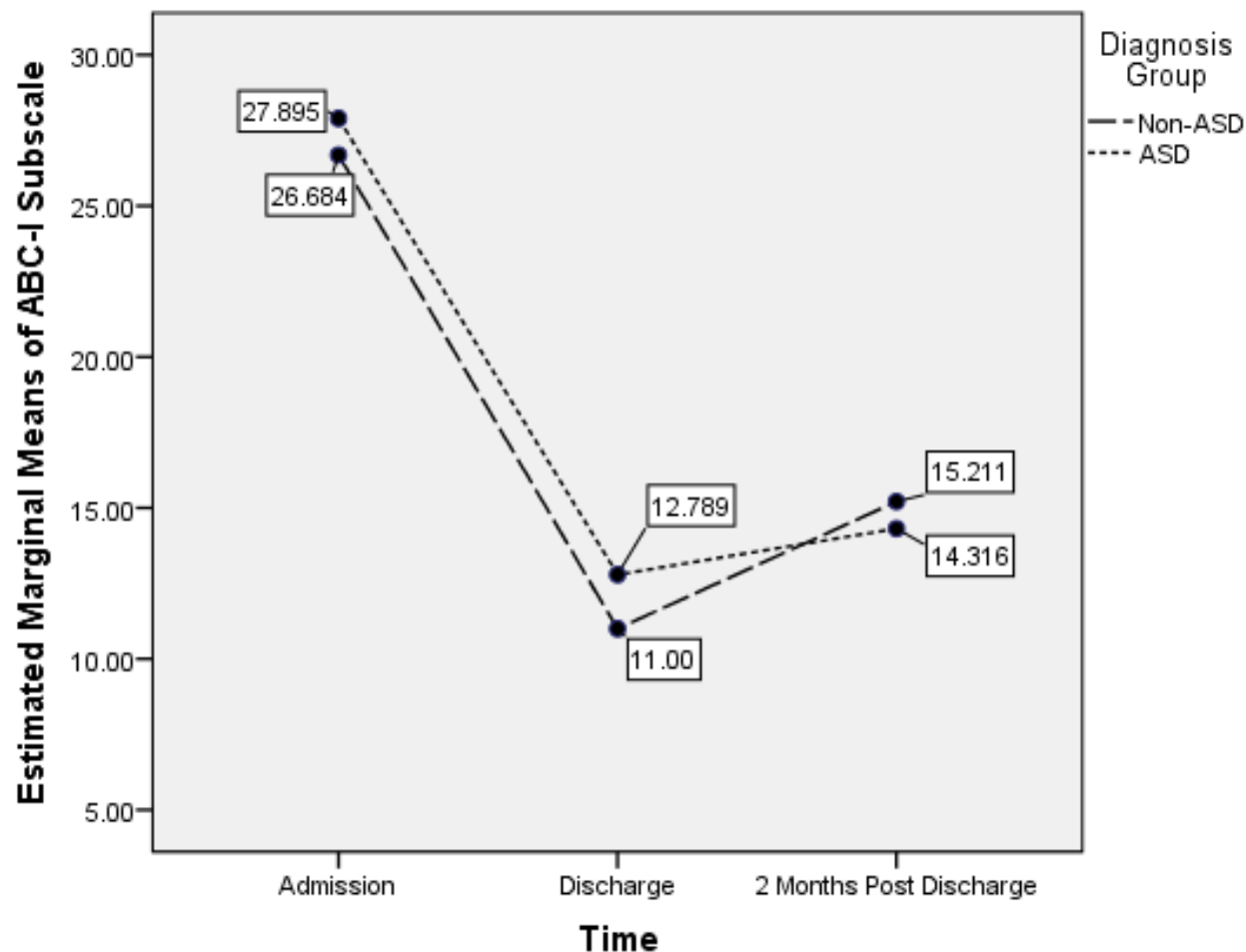
Significant side effects and inconsistent success

- Siegel M & Bealieu, A, *JADD*, 2011

- Communication strategies  
(AAC/Functional Communication)
- Treat Medical Problems
- Family treatment
- Parent Management Training (RUBI)
- Sensory regulation strategies
- Social skills / social cognitive strategies
- Psychotherapy approaches – CBT / Emotion regulation

# CHANGE IN BEHAVIORAL FUNCTIONING

Figure 1. Estimated Marginal Means of Abberant Behavior Checklist Irritability (ABC-I) Subscale Between Children with and without Autism Spectrum Disorder (ASD) Over Time



Siegel M, et al.,  
*JADD, July, 2014*



**ADDIRC** Autism & Development Disorders  
Inpatient Research Collaborative

**AIC** Autism  
Inpatient  
Collection



# AIC RATIONALE



Knowledge & treatment options continue to lag for those with autism who are non-verbal, have an intellectual disability and/or display challenging behaviors; under-represented in current, large data collections

- Communication: 30-50% do not develop functional verbal communication.
- Cognitive: 20-40% of individuals with Intellectual Disability (FSIQ<70)
- Behavioral: 20-30% with lifetime incidence of serious challenging behaviors

High volume of individuals - in a unique position to efficiently collect large amounts of data and improve understanding of this understudied portion of the ASD population

Inpatient setting an ideal platform to identify mechanisms underlying emotional and behavioral symptoms to inform treatment. Unique ability to study challenging behaviors *in situ* due to safety of inpatient environment and control over environmental factors

# AUTISM INPATIENT COLLECTION

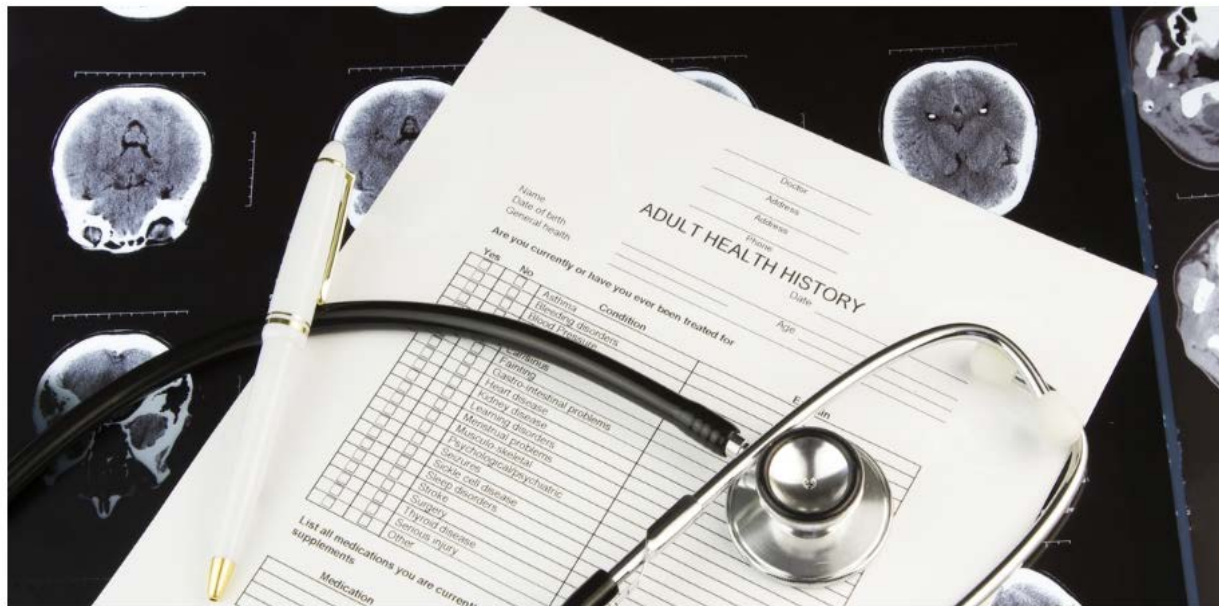


- **Goals:** Standardized assessment, description of the population, resource for all investigators, research platform for measure development, mechanistic studies and treatment studies.
  - To date, enrolled over 1000 probands and their biological parents
  - Rigorous core assessment battery and ASD diagnostic reliability
  - 48% minimally verbal, 42% Intellectual Disability (NVIQ <70; Molec Aut, 2015)
  - Whole exome sequencing to be performed 2018-19
  - Data available to approved investigators through SFARIBase
  - On-line community to facilitate recontacting through

**AUTISM INPATIENT  
COMMUNITY**  
@interactive autism network

# AIC ON SFARI BASE

## SFARI Base



How to access  
SFARI Base and  
request SFARI  
resources:

SFARI Base is a central database of phenotypic and genetic information about families affected by autism and other neurodevelopmental disorders, provided as part of the Simons Foundation Autism Research Initiative (SFARI). It contains data from the following cohorts:

- [Simons Simplex Collection \(SSC\)](#)
- [Simons Variation in Individuals Project \(Simons VIP\)](#)
- [Simons Foundation Powering Autism Research for Knowledge \(SPARK\)](#)
- [Autism Inpatient Collection \(AIC\)](#)



Predictors of  
Psychiatric  
Hospitalization

Inpatient  
Outcomes

Best practices for  
inpatient treatment

Psychotropic  
Medication  
Use

AIC  
Methods

Problem  
behaviors and  
verbal ability

Risk factors for  
Self-injurious  
behavior

Talking  
about death  
or suicide

Expression of  
Trauma

Sleep and  
problem  
behavior

Verbal ability and  
psychiatric  
symptoms

Development of  
the EDI

Anxiety

Sleep and caregiver  
stress

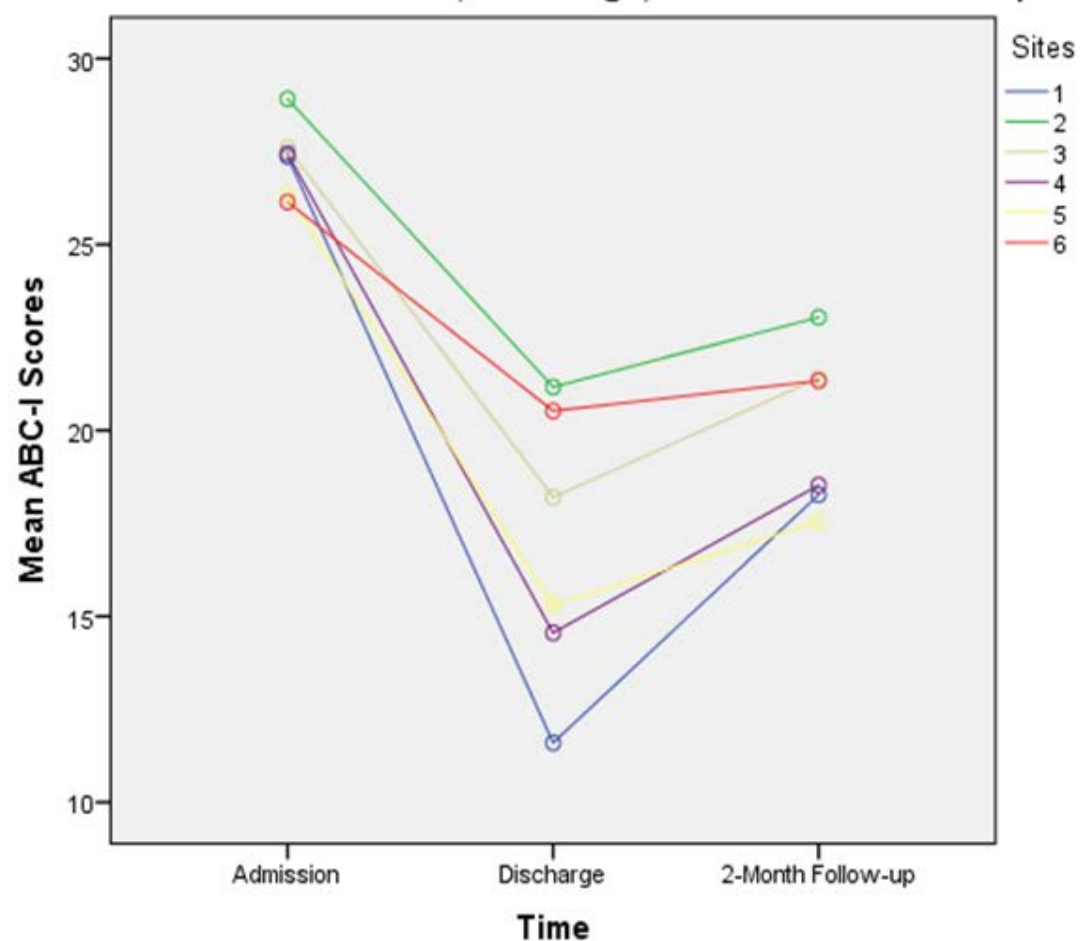
Health  
disparities

Parent stress  
and problem  
behavior

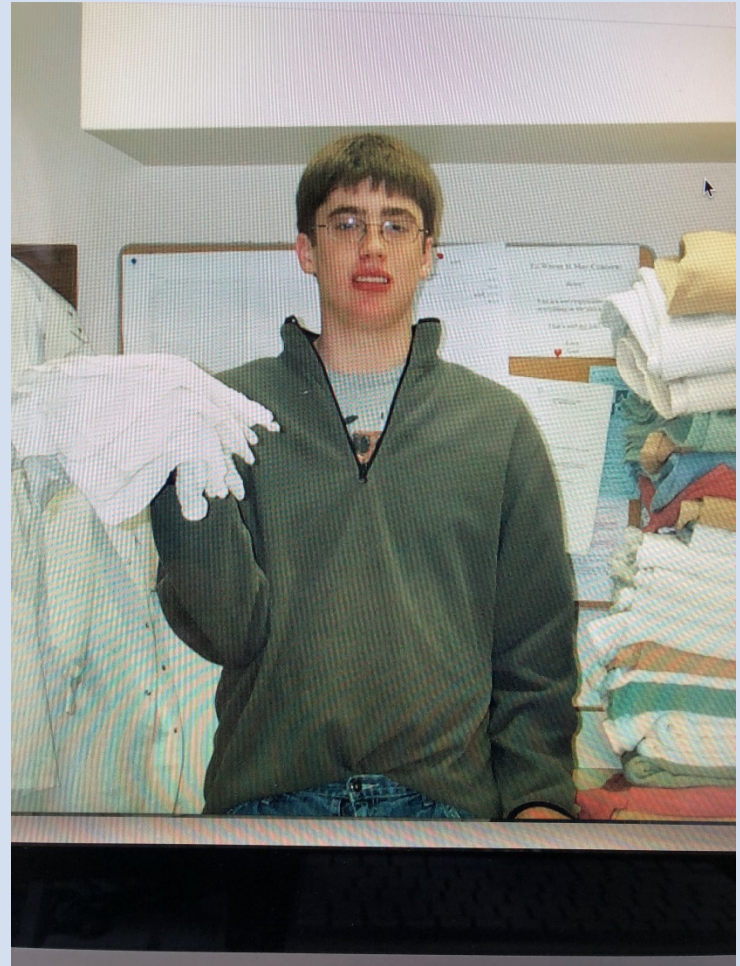
# AIC: CHANGE IN PROBLEM BEHAVIORS

## ABC-I Scores, n=350

- Significant reduction in problem behavior scores from admission to discharge, and 2-month follow-up ( $p \leq 0.05$ )
- Admission: 29.7(9.6)
- Discharge: 15.0(10.3)
- 2-Month Follow Up: 19.3(10.3)

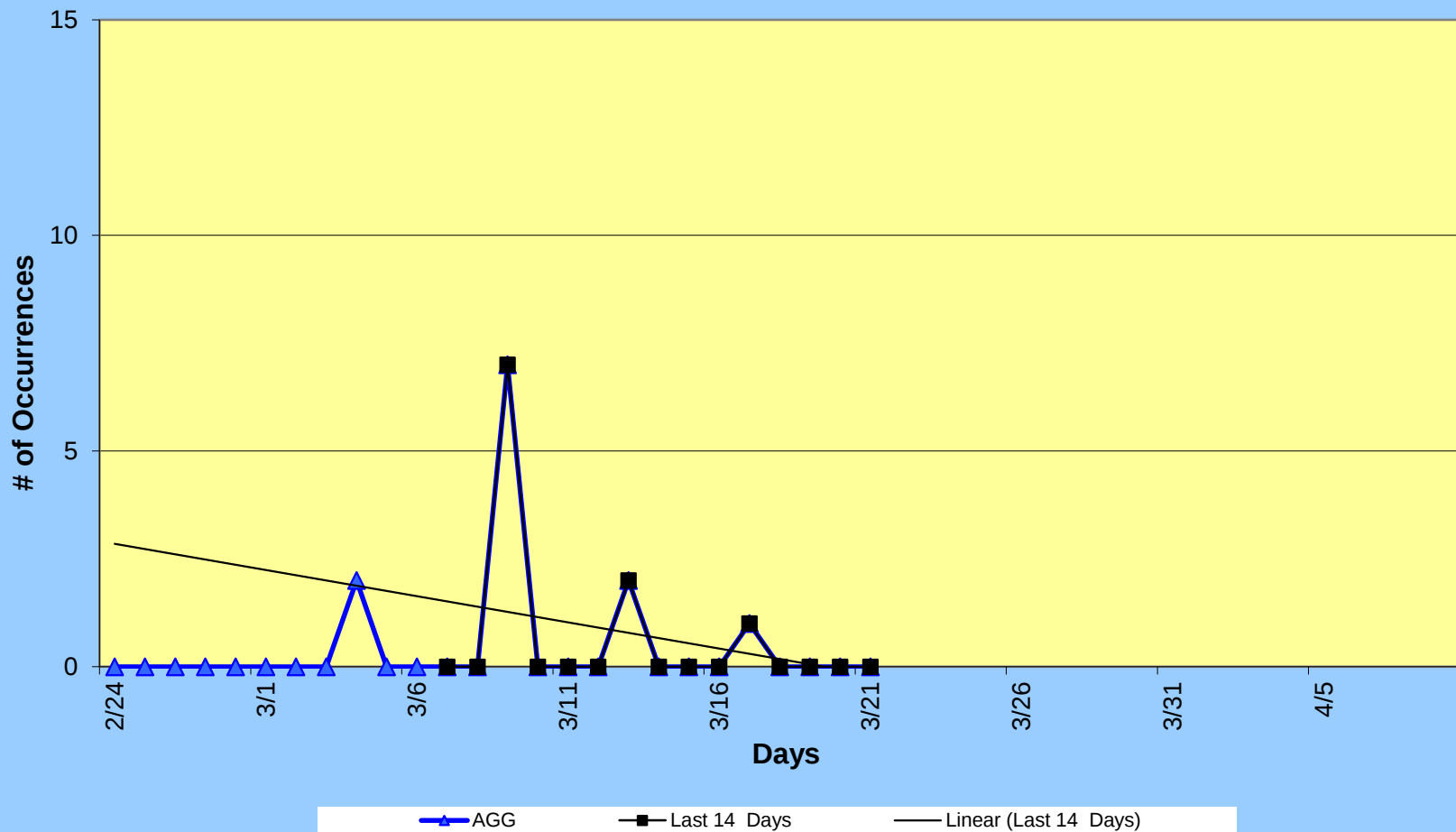


# RYAN – THE NEED FOR NOVEL APPROACHES



# IN HOSPITAL

## Ryan O's Aggression Over Stay 2011



# RYAN - 23 YEAR OLD MAN



“Due to his inability to manage his emotions and communicate, he attacks us when he becomes agitated or stressed. This behavior is very unpredictable and often occurs with little to no warning signs. It has happened in our home, his school, in the community and sometimes while driving a car. It is so bad that we can no longer safely live in our home with Ryan.”

-Wendi

# PHYSIOLOGICAL AROUSAL AND CHALLENGING BEHAVIOR

In typically developing youth, greater ability to modulate physiological arousal is associated with fewer behavior problems.

-Calkins SD. *Dev Psychobilly*. 1997;  
Porges, S.W. *Dev Psyche*; 1996

## Association between physiological arousal and problem behavior in ASD

- Cohen IL, et al., Assessing challenging behaviors in Autism Spectrum Disorders: Prevalence, rating scales, and autonomic indicators. In: *International handbook of autism and pervasive developmental disorders*. New York, NY: Springer; 2011;
- Groden J, et al, The impact of stress and anxiety on individuals with autism and developmental disabilities. In: *Behavioral Issues in Autism*. New York, NY: Springer; 1994;
- Romanczyk RG. Self-injurious behavior: Conceptualization, assessment, and treatment. In: *Advances in Learning & Behavioral Disabilities*. UK: Emerald Insight; 1986;
- Romanczyk RG, Lockshin S, O'Connor J. Psychophysiology and issues of anxiety and arousal. In: *Self-injurious Behavior*. New York, NY: Springer-Verlag; 1992

Hypothesis: Individual with ASD engages in a problem behavior as an attempt to alleviate distress and reestablish physiological homeostasis.

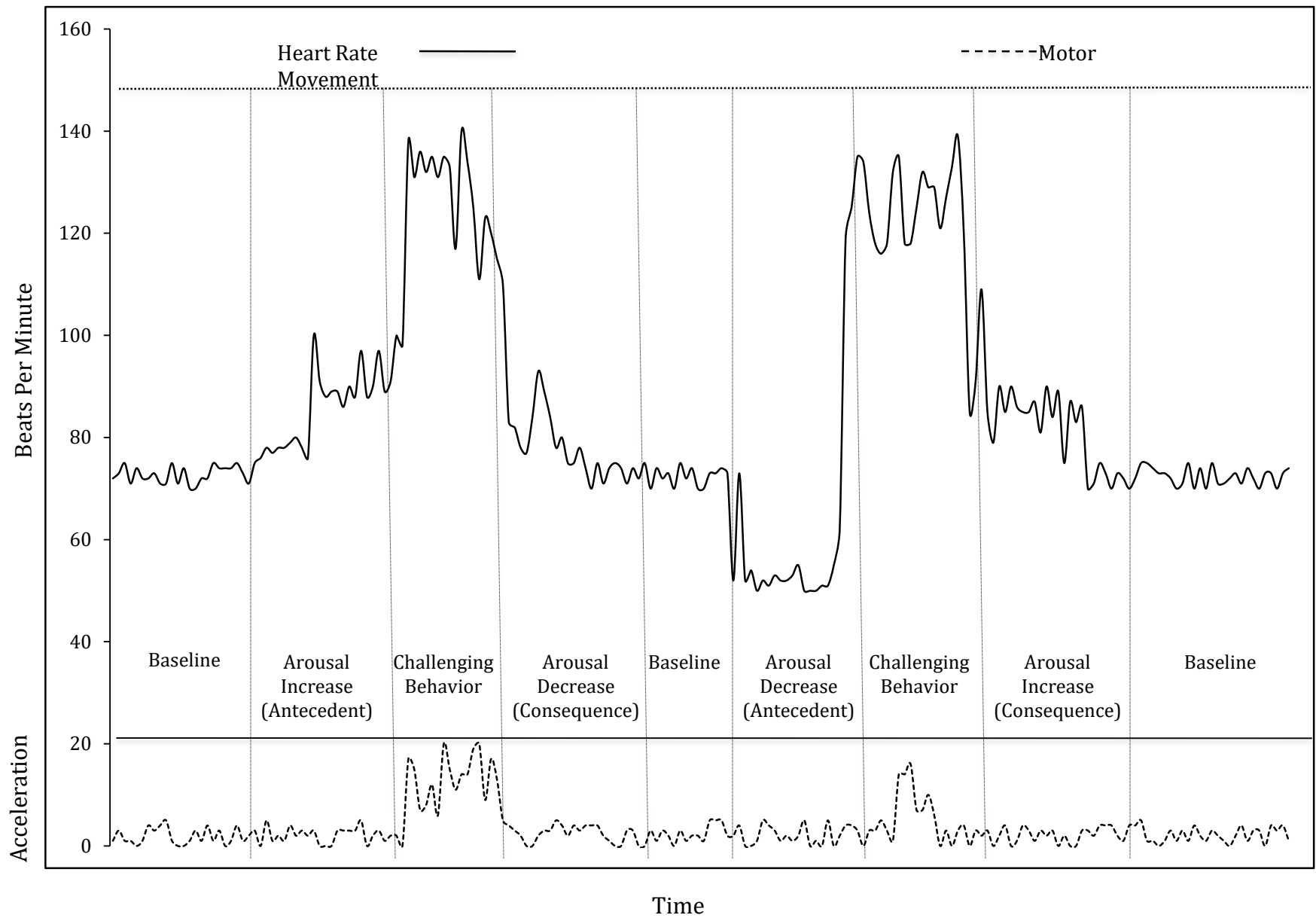
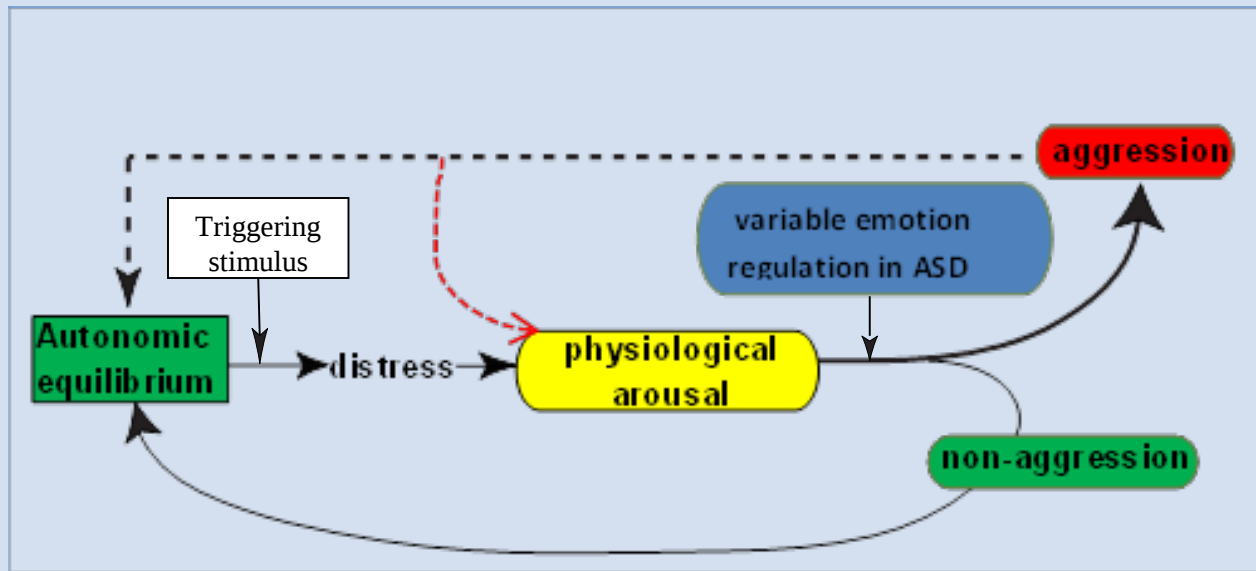
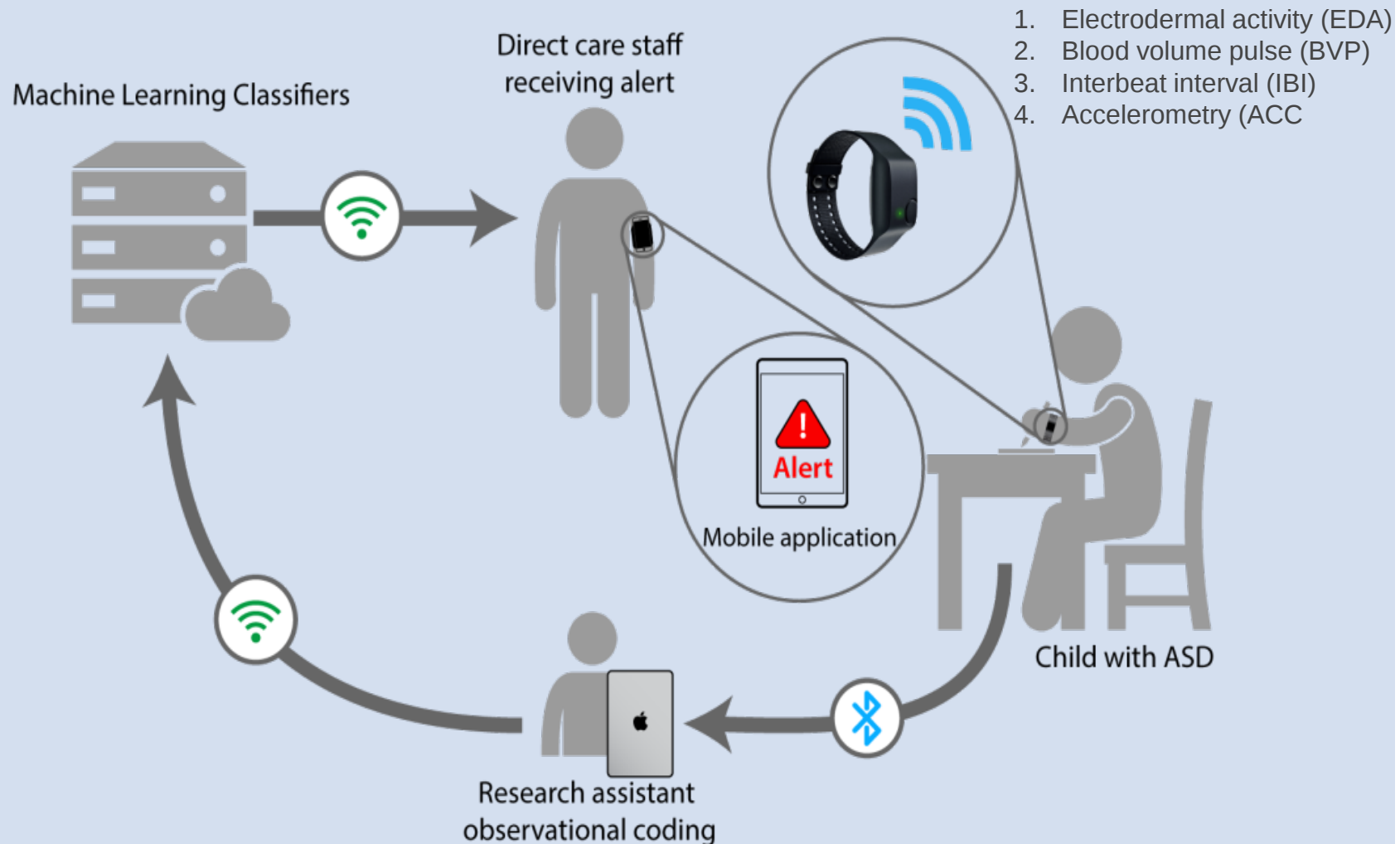


Figure by Matthew Goodwin, PhD

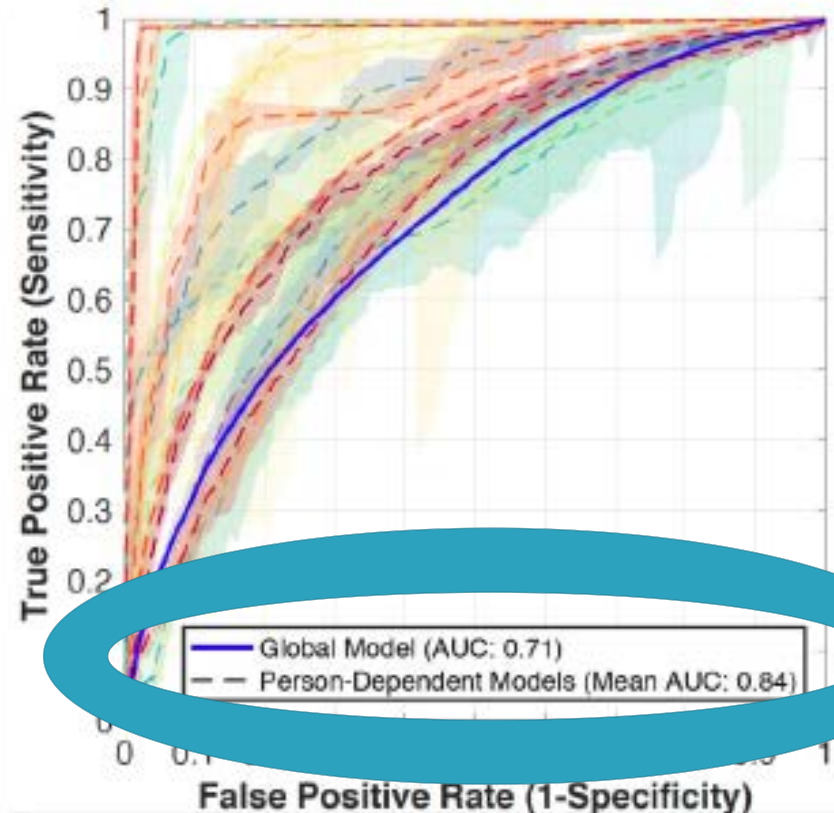
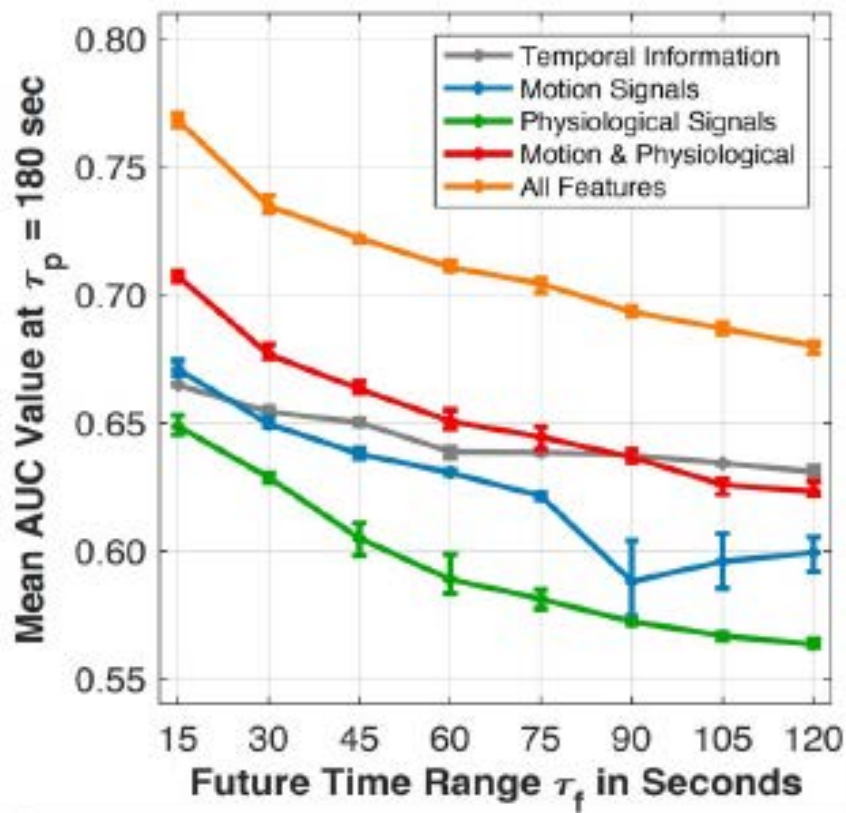
# CONCEPTUAL MODEL



# TRANSFORMING THE TREATMENT OF CHALLENGING BEHAVIOR – REAL TIME PREDICTION



# Pilot findings with 20 minimally-verbal inpatients



*AUC values as a function of time to aggression, and signals used from past 3 minutes of data*

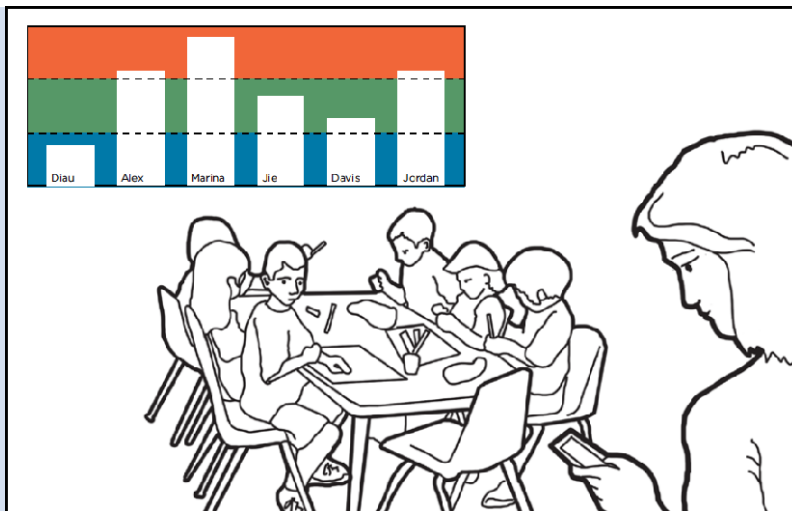
- ~80 hrs of collection over ~70 naturalistic observation sessions
- Increasing accuracy as you increase # of signal streams utilized

*ROC values for global and person-dependent models using all combined features from the past 3 minutes to predict the next 1 minute*

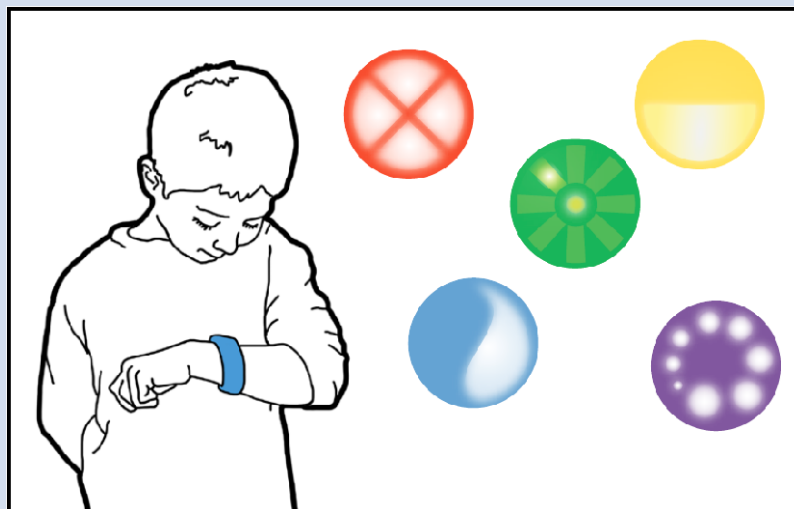
- Goodwin, MS, Ozdenizci, C, ... Mazefsky, C, Siegel, M, ... (in press). Predicting proximal aggression onset in minimally-verbal youth with autism spectrum disorder using preceding physiological signals. *Pervasive Health*.

- Ozdenizci, C, ... Mazefsky, C, Siegel, M, ... & Goodwin, MS (in press). Time-series prediction of proximal aggression onset in minimally-verbal youth with autism spectrum disorder using physiological biosignals. Accepted to 40<sup>th</sup> International Conference of the IEEE Engineering in Medicine and Biology Society.

## Staff Monitoring



## Self Monitoring



# CRITICAL UNMET RESEARCH NEEDS FOR THE SEVERELY AFFECTED

- Novel approaches to aggression and self injury that utilize objective, mechanistically-informed data
- Natural history of aggression and self-injury across the lifespan in ASD
- Validated, clinically practicable diagnostic tools for psychiatric co-morbidity
- Emotion regulation measurement and treatment
- Sleep biology and relationship to challenging behaviors
- Study of complex, real-world treatment packages (comparative effectiveness studies)
- Study of residential treatment and in-home behavioral services.

# SUMMARY

- Individuals with ASD can develop serious behavioral challenges, which can become more impairing than the ASD itself.
- Parents report it is the unpredictability and lack of warning that causes the greatest impairment.
- Aggression and self injury are under-researched, and their underlying biology not well understood, particularly in those who are minimally verbal or have intellectual disability
- Pilot data from the AIC suggests that measurement of physiological arousal, combined with other data streams, can be used to predict the proximal onset of aggression.
- Critical need for novel research approaches to the assessment and treatment of aggression, self-injury and other problem behaviors, focusing on objective, biological mechanisms and measures.

# ACKNOWLEDGEMENTS

## Site Co-Investigators

- **Carla Mazefsky, Ph.D, University of Pittsburgh**
- **Robin Gabriels, PsyD., Children's Colorado**
- **Giulia Righi, Ph.D. and Eric Morrow, MD, PhD, Brown University**
- **Craig Erickson, M.D. & Logan Wink, M.D., Cincinnati Children's**



## Maine Medical Center Research Institute

- **Susan Santangelo, Sc.D., Co-Investigator**
- **Kahsi A. Smith, Ph.D., Methodology/Statistics**
- **Mary Verdi, M.A., Project Manager**
- **Deanna Williams, B.A., Data Coordinator**
- **Christine Peura, B.A., Research Assistant**
- **Amy Stedman, B.A., Research Assistant**
- **Briana Taylor, PhD, Post-doctoral Fellow**
- **Donald St. Germain, M.D., Institute Director**

## Collaborators

- **Matthew Goodwin, Ph.D., Northeastern University**
- **Matthew Lerner, Ph.D. & Kenneth Gadow, Ph.D & SUNY Stonybrook**
- **Louis Haggopian, Ph.D., Kennedy Krieger Institute**
- **Diane Williams, Ph.D., Duquesne University**

## THE NANCY LURIE MARKS FAMILY FOUNDATION

*Fostering Knowledge and Community for Autism and Beyond*

## ADDIRC Scientific Advisory Group

Connie Kasari, PhD, UCLA  
Bryan King, MD, University of Washington  
James McCracken, MD, UCLA  
Christopher Mcdougale, MD, Harvard University  
Lawrence Scahill, Ph.D, MSN, Emory University  
Robert Schultz, Ph.D., University of Penn  
Helen Tager-Flusberg, Ph.D., Boston University