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TITLE: **Predicting Situational Onset of Aggression in Minimally Verbal Youth with Autism Using Biosensor Data and Machine Learning Algorithms**

PRINCIPAL INVESTIGATOR: Matthew Goodwin, PhD

CONTRACTING ORGANIZATION: Northeastern University

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Predicting Situational Onset of Aggression in Minimally Verbal Youth with Autism Using Biosensor Data and Machine Learning Algorithms

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6. AUTHOR(S)

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13. SUPPLEMENTARY NOTES

14. ABSTRACT

Unpredictable aggressive behavior by youth with autism spectrum disorder (ASD) isolates them from educational, social, and family activities. Approximately 2/3 of youth with ASD display aggression, a common reason for treatment referral; yet evidence-based pharmacological and behavioral interventions for aggression in ASD are frequently ineffective. Aggression is particularly impairing in the 30-40% of youth with ASD who are minimally verbal (MV-ASD). Aggression may represent a maladaptive attempt to express or modulate physiological arousal arising from distress. We hypothesize that physiological arousal precedes aggressive behavior. We aim to predict aggression in MV-ASD before it occurs using data collected from wrist-worn physiological sensors and behavior observation. Using sophisticated machine learning algorithms linking observable aggression to preceding physiological signals (heart rate, skin conductance), we may identify new opportunities for intervention.

15. SUBJECT TERMS
Autism Spectrum Disorder, ASD, Minimally Verbal, Aggression, Prediction, Physiological Arousal, Arousal Modulation, Machine Learning.

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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Unclassified	Unclassified	Unclassified	Unclassified	18	19b. TELEPHONE NUMBER *(include area code)*

TABLE OF CONTENTS

Page

1. INTRODUCTION: *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

Unpredictable and potentially dangerous aggressive behavior by youth with autism spectrum disorder (ASD) isolates them from important educational, social, and family activities, thereby increasing the difficulties and costs associated with the condition. As many as 2/3 of youth with ASD display aggression, which is one of the primary reasons they get referred for treatment. Aggression presents serious safety risks for the individual and others in the environment and frequently occurs with agitation, meltdowns, and other problem behaviors that are difficult to manage. Families report that aggression increases their stress, isolation, and financial burden, and decreases available support options. Aggression toward others is significantly impairing and challenging to manage in the 30-40% of youth with ASD who are minimally verbal (MV-ASD). Their difficulty verbalizing distress can lead to behaviors that seem to occur without warning, sometimes long after any obvious trigger. This unpredictability makes aggression toward others in MV-ASD dangerous and presents a barrier to accessing the community. Evidence-based pharmacological and behavioral interventions for ASD aggression are frequently ineffective due to significant medication side effects or insufficient time to provide de-escalation strategies. Aggression toward others may represent a maladaptive attempt to express or modulate physiological arousal arising from distress. Thus, we hypothesize that physiological arousal precedes aggressive behavior.

This project aims to predict aggression toward others in MV-ASD before it occurs using data collected from commercially available wrist-worn wireless physiological sensors. The unique inpatient setting where this study is taking place allows us to study aggression in a controlled, safe environment with 24-hour access to patients for an average of three weeks each. The project will provide predictive information (i.e., the onset of aggressive behavior in the proximal future using physiological data from the recent past) that may ultimately define new opportunities for intervention. This innovative approach has the potential to improve our ability to identify escalating distress in youth with MV-ASD, overcoming their inherent difficulty conveying feelings and emotions. By linking observable aggressive behavior to the detection of preceding physiological signals (e.g., heart rate, sweating), we hope to move the field of problem behavior assessment and treatment in autism towards a new biologically-based, data-informed approach that is focused on prospective monitoring, prevention, and eventually, real-time intervention.

2. KEYWORDS: *Provide a brief list of keywords (limit to 20 words).*

Autism Spectrum Disorder, ASD, Minimally Verbal, Aggression, Prediction, Physiological Arousal, Arousal Modulation, Machine Learning.

3. ACCOMPLISHMENTS: *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Goal 1: Establish physiological biomarkers of imminent aggression. We will observe and record aggression toward others in 40 MV-ASD inpatient youth during repeated naturalistic observations in an inpatient psychiatric unit while they wear validated wireless autonomic biosensors that measure physiological arousal (i.e., cardiovascular and electrodermal) and motor activity. These data, in combination with time-synchronized coding of aggression and non-aggression by research staff using a mobile application, will be analyzed by machine learning algorithms to create a set of properties (a "classifier") that predict imminent aggression (i.e., the onset of aggressive behavior in the proximal future using physiological data from the recent past).

Goal 2. Evaluate the positive predictive value and reliability of imminent aggression prediction. We will apply the highest performing classifiers from Aim 1 to validate aggression prediction prospectively in an independent MV-ASD inpatient youth sample (n=20) and examine classifier performance and individuals' stability over time.

What was accomplished under these goals?
For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

No data was received from the Partnering PI during the funding period. While COVID-19 may explain a delay, I have yet to hear a reason for the absence of any shared data.

The proposal funded 60 MV-ASD cases over the three-year period.

At the end of Y1, the proposal stated 21 cases by Q4 would be sent to me by the Partnering PI. After I reviewed the Y1 annual technical report, I inquired with the Partnering PI why only 8 cases had been completed when 21 were expected. He stated that they were having trouble recruiting participants with MV-ASD. I understood that once his recruiting issues were resolved I would receive the 8 cases reported plus the 13 owed.

At the end of Y2, the proposal stated 46 cases by Q4 would be sent to me. After I reviewed the Y2 annual technical report, I inquired why only 10 cases were reported completed. I was told COVID-19 had reduced clinical admissions.

During Y3 the Partnering PI advised he was requesting a protocol change with the DOD to shift participant recruitment criteria from MV-ASD to verbal ASD with intellectual disability (ID). I thought if this protocol change was granted that additional cases would be forthcoming. This protocol change was granted.

At the end of Y3, the Partnering PI filed an annual report without copying me.

I received a request from the DOD Program Officer to file a Y3 annual report in light of a recent No-Cost Extension (NCE) that was approved. I requested from the Partnering PI a copy of the Y3 annual report he submitted and was told by his Project Manager "I am unable to provide this document currently."

The DOD Program Officer provided me a copy of the Partnering PI's submitted Y3 annual report. While I haven't had the opportunity to review it thoroughly, it claims that 25 cases have been completed to date.

I have not received any of these 25 completed cases as of the date of this report.

As a result, no research into machine learning classification/behavioral prediction with the funded data has occurred.

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Nothing to Report.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Nothing to Report.

What do you plan to do during the next reporting period to accomplish the goals?
If this is the final report, state "Nothing to Report."

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

Without the funded data, any of the goals to be accomplished as a result of receipt of data from the Partnering PI are not attainable due to do lack of data supply.

However, research regarding machine learning/behavioral prediction can be accomplished using data available to me prior to funding. A detailed description can be found in the Northeastern University NCE "Work to Be Done During One Year Extension." This was the paragraph I drafted to explain my work during the NCE.

4. IMPACT: D*escribe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

Nothing to Report.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to Report.

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:
- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to Report.

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as: improving public knowledge, attitudes, skills, and abilities; changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or improving social, economic, civic, or environmental conditions.

Nothing to Report.

5. CHANGES/PROBLEMS: *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

Changes in approach and reasons for change
Describe any changes in approach during the reporting period and reasons for these changes. Remember that significant changes in objectives and scope require prior approval of the agency.

There are no significant changes in the direction and scope of my machine learning/behavior prediction research. However, I have ended my reliance on data from the Partnering PI due to performance issues. For example, I forfeited an NCE funded by a private foundation involving the Partnering PI that occurred after the DOD NCE was approved.

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

The absence of data provided by the Partnering PI to me over a three-year period has created a lost opportunity to advance my machine learning/behavior prediction research. When a partner was encountering problems supplying the funded data I chose to believe his obstacles were real and trusted his stated endeavors to correct them. I now see this belief and trust was misplaced. This is why I did not participate in the privately funded NCE.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to Report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to Report.

Significant changes in use or care of vertebrate animals

Nothing to Report.

Significant changes in use of biohazards and/or select agents

Nothing to Report.

6. PRODUCTS: *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**

Report only the major publication(s) resulting from the work under this award.

Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report related to the data promised but not provided.

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report related to the data promised but not provided.

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to Report related to the data promised but not provided.

- **Website(s) or other Internet site(s)**

List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to Report.

- **Technologies or techniques**

Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to Report related to the data promised but not provided.

- **Inventions, patent applications, and/or licenses**

Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to Report.

- **Other Products**

Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:

- *data or databases;*
- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to Report related to the data promised but not provided.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Name:	*Matthew Goodwin*
Project Role:	*PI*
Researcher Identifier (e.g. ORCID ID):	*0000-0002-4237-601X*
Nearest person month worked:	*1*
Contribution to Project:	*No change.*
Funding Support:	*The Simons Foundation and Nancy Lurie Marks Foundation provided additional, complementary support toward this project, as explained in materials submitted to the DoD; these foundations provide additional funding to open more sites and enroll more patients.*

Name:	*Efstratios Ioannidis*
Project Role:	*Co-I*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*1*
Contribution to Project:	*Supervised machine learning analyses performed by Post Doc and graduate students at NU using N=20 data set, the precursor to this funding.*
Funding Support:	

Name:	*Tales Imbiriba*
Project Role:	*Post Doc*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*3*
Contribution to Project:	*Performed machine learning analyses on N=20 data set, the precursor to this funding.*
Funding Support:	

Name:	*Ahmet Demirkaya*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*8*
Contribution to Project:	*Performed machine learning analyses on N=20 data set, the precursor to this funding.*
Funding Support:	

Name:	*Natasha Yamane*
Project Role:	*Graduate Student*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*4*
Contribution to Project:	*Assisted with machine learning analyses preformed on machine learning analyses on N=20 data set, the precursor to this funding.*
Funding Support:	

Name:	*Diana Cumpanasoiu*
Project Role:	*PhD student*
Researcher Identifier (e.g. ORCID ID):	
Nearest person month worked:	*1*
Contribution to Project:	*No change*
Funding Support:	

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

New Award.

Title: Physiological mechanisms of action relating to immediate and long-term therapeutic horseback riding intervention effects in a psychiatric population of youth with autism spectrum disorder.

Role: Goodwin Co-investigator

Project Number: 1 R01 HD097693-01A1

Source: Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

Goals: This randomized control trial (RCT) seeks to assess the physiological mechanisms underlying Therapeutic Horseback Riding's (THR) previously observed significant positive effects on ASD youth, particularly those with co-occurring psychiatric disorders, and to refine information on the durability, dose and subpopulation effects of the intervention.

12/1/19 - 11/30/24

0.60 calendar Yr 1-4
3.60 calendar Yr 5

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)
- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Nothing to Report.

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to* ***https://ers.amedd.army.mil*** *for each unique award.*

QUAD CHARTS: *If applicable, the Quad Chart (available on https://www.usamraa.army.mil) should be updated and submitted with attachments.*

Enclosed.

9. APPENDICES: *Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.*

Nothing to Report.

Predicting Situational Onset of Aggression in Minimally Verbal Youth with Autism Spectrum Disorder Using Biosensor Data and Machine Learning Algorithms

ERMS/Log Number AR170209P1

Award Number W81XWH-18-1-0459 Annual Research Performance Progress Report

PI: Matthew Goodwin, PhD **Org:** Northeastern University **Award Amount:** $460,733

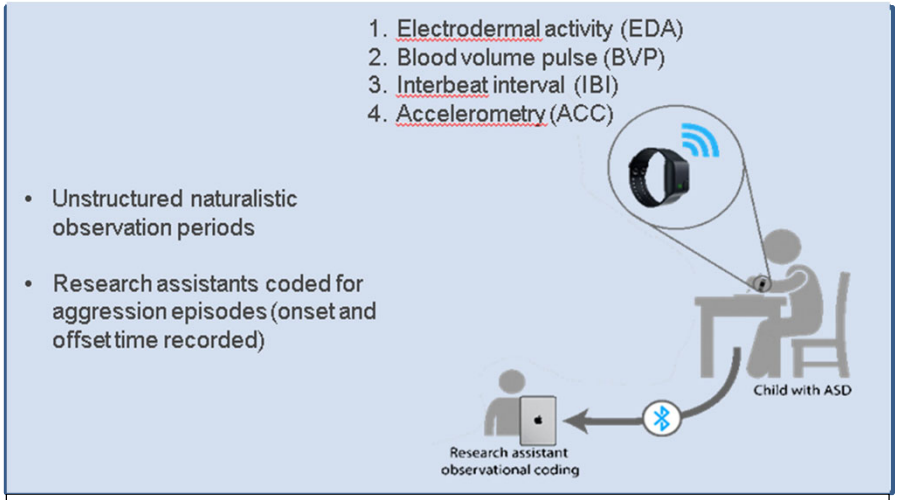
Study/Product Aim(s)

• Aim 1: Establish physiological biomarkers of imminent aggression in minimally verbal youth with Autism Spectrum Disorder (MV-ASD).

• Aim 2: Evaluate the positive predictive value and reliability of imminent aggression prediction.

Approach

Toward Aim 1, we will observe and record aggression in 40 MV-ASD youth in an inpatient psychiatric unit while they wear wireless autonomic biosensors that measure physiological arousal. These data, in combination with time-synchronized coding of aggressive behavior, will be analyzed by machine learning algorithms to create a set of properties to predict imminent aggression ('classifier'). To achieve Aim 2, we will apply the highest performing classifiers from Aim 1 to validate aggression prediction prospectively in an independent MV-ASD inpatient youth sample (n=20) and examine classifier performance and stability within individuals over time.



Depicted is our data collection model, measuring physiological arousal (EDA, IBI & ACC using the E4 sensor) as a predictive biomarker for onset of aggressive behavior.

Timeline and Cost

Activities Funding year	2018/2019	2019/2020	2020/2021
Refine data collection procedures and establish aggression detection reliability			
Enroll & collect data from 40 participants to develop prediction classifier			
Analyze data using machine learning algorithms to optimize classifier			
Collect data with 20 additional subjects to validate aggression prediction model			
Estimated Budget ($K)	**152,347**	**158,825**	**151,561**

Updated: This is the second Quad chart for this award

Goals/Milestones

Year one goals- Launch and collect aggression and physiological data

☑ Train research staff and demonstrate aggression detection reliability

☑ Develop database and system for physiological data transfer to Northeastern machine learning team

☑ Implement quality checks to optimize collection of high-quality sensor data

☑ Enroll and collect behavior and physiological data with MV-ASD youth

Year two goals- Develop classifier

☒ Continue data collection to achieve N of 40 minimally verbal ASD youth

☐ Begin collection of data with 20 additional MV-ASD youth for Aim 2

☒ Quarterly re-calibration to confirm reliability of ≥80% for aggression detection

☐ Apply machine learning algorithms to data for first 40 participants to develop aggression prediction classifier

Year three goals- Validate classifier

☐ Complete data collection and test classifier for prediction of aggression in 20 final participants

Comments/Challenges/Issues/Concerns

No data from Partnering PI for Aim 1 and 2 have been received to date.

Budget Expenditure to Date

Projected Expenditure: $460,733

Actual Expenditure: $367,310