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RESEARCH ARTICLE

Predicting Aggression to Others in Youth With Autism Using a Wearable Biosensor

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Unpredictable and potentially dangerous aggressive behavior by youth with Autism Spectrum Disorder (ASD) can isolate them from foundational educational, social, and familial activities, thereby markedly exacerbating morbidity and costs associated with ASD. This study investigates whether preceding physiological and motion data measured by a wrist-worn biosensor can predict aggression to others by youth with ASD. We recorded peripheral physiological (cardiovascular and electrodermal activity) and motion (accelerometry) signals from a biosensor worn by 20 youth with ASD (ages 6–17 years, 75% male, 85% minimally verbal) during 69 independent naturalistic observation sessions with concurrent behavioral coding in a specialized inpatient psychiatry unit. We developed prediction models based on ridge-regularized logistic regression. Our results suggest that aggression to others can be predicted 1 min before it occurs using 3 min of prior biosensor data with an average area under the curve of 0.71 for a global model and 0.84 for person-dependent models. The biosensor was well tolerated, we obtained useable data in all cases, and no users withdrew from the study. Relatively high predictive accuracy was achieved using antecedent physiological and motion data. Larger trials are needed to further establish an ideal ratio of measurement density to predictive accuracy and reliability. These findings lay the groundwork for the future development of precursor behavior analysis and just-in-time adaptive intervention systems to prevent or mitigate the emergence, occurrence, and impact of aggression in ASD. ***Autism Res*** *2019, 12: 1286–1296*. © 2019 International Society for Autism Research, Wiley Periodicals, Inc.

Lay Summary: Unpredictable aggression can create a barrier to accessing community, therapeutic, medical, and educational services. The present study evaluated whether data from a wearable biosensor can be used to predict aggression to others by youth with autism spectrum disorder (ASD). Results demonstrate that aggression to others can be predicted 1 min before it occurs with high accuracy, laying the groundwork for the future development of preemptive behavioral interventions and just-in-time adaptive intervention systems to prevent or mitigate the emergence, occurrence, and impact of aggression to others in ASD.

Keywords: aggression; autism spectrum disorder; inpatients; autonomic nervous system; biosensing techniques

Introduction

The purpose of the present study is to evaluate whether peripheral physiological arousal and motion data measured by a wearable biosensor can be used to predict aggression to others by youth with autism spectrum disorder (ASD). ASD is one of the most common childhood disorders (1 in 59) [Baio et al., 2018] and it is associated with high health care cost [Amendah, Grosse, Peacock, & Mandell, 2011]. While ASD is characterized by social communication impairments and restricted, repetitive behaviors and interest [American Psychiatric Association, 2013], youth with ASD are also at increased risk for a range of co-occurring psychiatric and behavioral issues compared to the general population [Gray et al., 2012; Joshi et al., 2010; Leyfer et al., 2006; Salazar et al., 2015; Simonoff et al., 2008]. Aggression is one of the most frequently observed problem behaviors in youth with ASD [Kanne & Mazurek, 2011; Matson & Cervantes, 2014], especially in the more severely affected [Bronsard, Botbol, & Tordjman, 2010; Matson & Rivet, 2008; McClintock, Hall, & Oliver, 2003; Tsiouris, Kim, Brown, & Cohen, 2011], and ranks among the most common causes for referral to behavioral healthcare services [Arnold et al., 2003]. Physical aggression, including hitting, biting, scratching, and throwing objects at others, is particularly debilitating because it often occurs without warning, sometimes long after any observable trigger, creating an environment of unpredictability.

Unpredictable aggression can create a barrier to accessing community, therapeutic, medical, and educational services. For instance, families report that aggression increases their stress, isolation, and financial burden,

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and decreases available support options because they are understandably afraid to put their child with ASD into potentially stressful environments that might lead to aggression without warning [Davis & Carter, 2008; Hodgetts, Nicholas, & Zwaigenbaum, 2013]. Frequent aggression can also have deleterious effects on professional support providers, leading to increased sick days, higher turnover rates, and compensatory payments for injury [Allen, 2000; Kiely & Pankhurst, 1998]. This predicament can demoralize parents and providers, accelerate negative patient trajectories, and lead to homebound or residential living placement, collectively decreasing quality of life while increasing healthcare costs [Jewett, 2017; Price & Price, 2016]. Cross-sectional and longitudinal studies suggest that even though aggression may decline in ASD over the lifespan, it can persist into adulthood and remains heightened in comparison to typically developing and intellectually impaired populations without ASD [Farmer & Aman, 2009, 2011; Gray et al., 2012; Woodman, Mailick, & Greenberg, 2016].

Aggression is often treated with medication, which can be efficacious in some instances but can also have significant side effects and inconsistent success [Adler et al., 2015; Williamson et al., 2017; Wink, Pedapati, Horn, McDougle, & Erickson, 2017]. Applied Behavior Analysis (ABA) has also been shown to be effective at reducing aggression and other problem behaviors in youth with ASD [Doehring, Reichow, Palka, Phillips, & Hagopian, 2014]. Primary mechanisms utilized by ABA are identification and control of antecedents, motivating operations, and consequences that either occasion or reinforce behavior. However, identifying these factors can be challenging (particularly when they are internally mediated and the respondent cannot verbalize his or her experience; Carr & Owen-Deschryver, 2007), is time-intensive, and often requires extensive specialized expertise that is not readily accessible to most families [Xu et al., 2018].

Physiological arousal is a potentially promising objective indicator that may precede aggression toward others. Physiological arousal is consistently implicated in aggression [Lindsay & Anderson, 2000]. In typically developing youth, greater ability to regulate physiological arousal is associated with fewer behavior problems [Calkins, 1997; Porges, 1996]. Studies of psychiatric disorders characterized by emotional and behavioral dysregulation, such as bipolar disorder and antisocial behavior, report a strong association between physiological arousal and symptomatology [De Vries-Bouw et al., 2011; Lorber, 2004; Ortiz & Raine, 2004; Raine, 2002]. Some of the earliest descriptions of ASD highlight atypical physiological arousal, including the supposition that problem behaviors are functionally related to homeostatic regulation [DesLauriers & Carlson, 1969; Hutt & Hutt, 1965; Kinsbourne, 1980; Ornitz & Ritvo, 1968; Rimland, 1964]. While significant heterogeneity in individuals with ASD exists, recent reviews demonstrate that atypical autonomic reactivity is a common feature [Klusek, Roberts, & Losh, 2015; Levine, Conradt, Goodwin, Sheinkopf, & Lester, 2014; Lydon et al., 2016] and can putatively occasion maladaptive behavior when demands exceed an individual's coping ability [Cohen, Yoo, Goodwin, & Moskowitz, 2011; Scarpa, 2015]. Given the aforementioned literature, the purpose of the present study is to test the hypothesis that preceding changes in physiological arousal can be used to accurately predict aggression before it occurs.

Methods

Participants

Twenty psychiatric inpatients with confirmed ASD were serially enrolled at one site of the Autism Inpatient Collection (AIC) study and initiated our aggression prediction protocol. The AIC is an ongoing six-site study of over 1,200 children, adolescents, and young adults admitted to specialized inpatient psychiatric units for persons with ASD and other developmental disorders. The full methods of the AIC study have been published previously [Siegel et al., 2015]. Briefly, patients 4–20 years old with a score of ≥12 on the Social Communication Questionnaire [Rutter, Bailey, & Lord, 2003] or high suspicion of ASD from the inpatient clinical treatment team were eligible for enrollment. Inclusion criteria required confirmation of ASD diagnosis by research-reliable administration of the Autism Diagnostic Observation Schedule-2 (ADOS-2) [Lord et al., 2012]. Exclusion criteria included not having a parent available who was proficient in English or the individual with ASD having prisoner status. Within 10 days of admission, a primary caregiver of the participant completed the Aberrant Behavior Checklist (ABC) [Aman, Singh, Stewart, & Field, 1985], Child Behavior Checklist (CBCL) [Achenbach, 1991], Vineland Adaptive Behavior Scales-2 (VABS-2) [Sparrow, Balla, & Cicchetti, 1984], and Emotion Dysregulation Inventory (EDI) [Mazefsky, Yu, White, Siegel, & Pilkonis, 2018]. Participants were also administered the Leiter-3 test of nonverbal intelligence [Roid & Koch, 2017].

The 20 participants in the present aggression prediction study were 6–17 years old (M = 10.8, SD = 3.1) and were predominantly male (75%), white (95%), and non-Hispanic (90%) (Table 1). Most were minimally verbal (85% ADOS-2 module 1 or 2) and had intellectual disability (Leiter-3 nonverbal IQ score M = 66.1, SD = 9.0). Mean scores on the CBCL were consistently in the borderline clinical or clinical range across psychiatric diagnostic categories. Mean VABS-2 scores in the domains of daily living skills, communication, and socialization were consistently in the severely impaired range. Average ABC subscale scores were very elevated, indicating a high frequency and severity of aggression, self-injury, and tantrums (ABC-irritability subscale M = 28.4, SD = 8.7) as well other

Table 1. Sample Characteristics

Demographics	
Age	10.8 ± 3.1
Sex, Male - *N* (%)	15 (75.0)
Race, White - *N* (%)	19 (95.0)
Ethnicity, non-Hispanic - *N* (%)	18 (90.0)
Minimally or nonverbal - *N* (%)	17 (85.0)
Leiter nonverbal IQ	66.1 ± 19.0
Length of stay (in days)	57.8 ± 27.7
Child Behavior Checklist - DSM Oriented Scales (t-scores)[a]	
Depressive problems	71.9 ± 4.7
Oppositional defiant problems	68.7 ± 7.5
Conduct problems	66.0 ± 5.4
Attention deficit/hyperactivity problems	64.5 ± 5.7
Anxiety problems	62.3 ± 7.8
Somatic problems	60.1 ± 7.1
Vineland Adaptive Behavior Scales (standard scores)[b]	
Daily living skills	55.6 ± 10.8
Communication	53.0 ± 9.0
Socialization	50.2 ± 9.6
Vineland Adaptive Behavior Scales (v-scale scores)[b]	
Maladaptive behavioral index	21.8 ± 1.3
Internalizing	22.0 ± 1.0
Externalizing	20.2 ± 1.4
Aberrant Behavior Checklist at Admission	
Irritability[b]	28.4 ± 8.7
Stereotypy[c]	8.3 ± 5.5
Lethargy[c]	13.7 ± 6.8
Hyperactivity[c]	26.1 ± 7.2
Inappropriate speech[c]	3.8 ± 3.9
Emotion dysregulation inventory at admission (t-scores)	
Reactivity[d]	58.3 ± 8.2
Dysphoria[c]	54.9 ± 8.2

[a] *N* = 15.
[b] *N* = 18.
[c] *N* = 19.
[d] *N* = 17.

problem behaviors. EDI reactivity (*t*-score *M* = 58.3, *SD* = 8.2) and dysphoria (*t*-score *M* = 54.9, *SD* = 8.2) scores were in the average range compared to the EDI's large autism psychometric sample [Mazefsky et al., 2018], and two and one *SD* higher, respectively, than a general sample of 1,000 US census-matched youth [Mazefsky, Yu, White, & Pilkonis, 2019].

Both the AIC and aggression prediction protocols were approved by the IRB of the participating study site, and the guardians of all participants provided informed consent. The AIC phenotypic data are available to external investigators through SFARI Base (www.sfari.org/resource/sfari-base/), and soon will include genetic sequencing data.

Aggression Prediction Protocol

Sixty-nine naturalistic observation sessions totaling 87 hr were performed by research staff in the inpatient unit while participants wore a wireless biosensor. Biosensor data collection began on average 45 days (*SD* = 40) since time of admission, for an average of 10 consecutive days (*SD* = 10), over an average 91 days (*SD* = 50) of inpatient stay. Research staff conducted these observations with minimal interference to participants' daily inpatient routines, which consisted of academic lessons, behavioral, occupational, speech and milieu therapies, meals, and free time. Research staff coded the start and stop times of each aggression episode within the observation period using a laptop computer time-synchronized to the internal clock of the biosensor worn by the participant. Aggression was operationally defined as hitting, kicking, biting, scratching, grabbing, pulling, pinching, or throwing objects at others.

Wearable Biosensor

Peripheral physiological arousal and motion activity were collected from participants using the commercially available and regulatory compliant E4 by Empatica, Inc. The E4 weighs 40 g and is made of durable polyurethane and polycarbonate materials that make it water and shockproof. It uses photoplethysmography (PPG) [Allen, 2007] to record blood volume pulse (BVP) and Inter-Beat-Interval (IBI) data at 64 Hz, from which heart rate and heart rate variability (a measure of variation in the beat-to-beat interval [Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, 1996]) can be derived. Differences in PPG as a result of skin color and external light intensity are dynamically compensated for by device firmware. Device firmware also includes motion artifact removal and IBI detection algorithms that automatically discard non-prototypical beats without smoothing IBI sequences. The E4 records electrodermal activity (EDA) at 4 Hz with a 0.01–100 microSiemen range, reflecting autonomic innervation of sweat glands and alterations in sympathetic nervous system arousal [Boucsein, 2012; Critchley, 2002]. Finally, the E4 records motion-based activity up to ±8 g at 32 Hz using a 3-axis accelerometer (ACCx, ACCy, and ACCz). Core sensing technologies in the E4 have been validated against gold standard laboratory-based devices during physical activity, emotional provocation, and high cognitive load in typically developing individuals [Poh, Swenson, & Picard, 2010].

Time-Series Feature Extraction

We extracted the following E4 time-series features for BVP, IBI, EDA, ACCx, ACCy, and ACCz using successive 15-sec sliding windows: first, last, maximum, minimum, mean, and median value; amount of unique values; and sum, standard deviation, and variance of values falling in a window. We also extracted the following two binary aggression labels provided by research staff coding: aggression observation flag (AOF; indicating when an aggression has occurred) and time since past aggression (TPA; indicating time elapsed since the last observation of aggression). The *SD* of each extracted feature was also included in all prediction models.

Logistic Regression Classifier Model

Ridge-regularized logistic regression was used with extracted time-series features as input variables to make binary aggression predictions over time. Specifically, at every time point t the classifier estimated whether aggression will be observed or not, indicated by label l, in an upcoming time range $(t, t + \tau_f)$ using features extracted in a previous time range $(t - \tau_p, t)$. Samples were split into training and testing datasets using fivefold cross-validation, repeated five times to produce confidence intervals (CI). At each fold, the classifier was trained via maximum likelihood estimation for optimal ridge-regularized regression weights $\boldsymbol{\beta} = [\beta_0, \beta_1, \ldots, \beta_d]^{\mathrm{T}}$, where d is the number of features. For prediction, the classifier generates probabilities for two classes $l = +1$ (aggression) and $l = -1$ (non-aggression) in the form:

$$P(l = +1 | \boldsymbol{x}; \boldsymbol{\beta}) = \frac{1}{1 + \mathrm{e}^{-\beta T x}},$$

where $\boldsymbol{x} = [1, x_1, \ldots, x_d]^{\mathrm{T}}$ and corresponds to the concatenated feature vector from $(t - \tau_p, t)$. Receiver operator characteristic (ROC) curves and corresponding area under the curve (AUC) values were calculated to assess decision thresholds over these probabilities.

The following five feature (signal) subsets were used as predictor variables (x) in our analyses: (a) only temporal information (AOF, TPA); (b) only motion activity (ACC); (c) only physiological activity (BVP, IBI, and EDA); (d) motion and physiological activity features combined (BVP, IBI, EDA, and ACC); and (e) all extracted features combined (AOF, TPA, ACC, BVP, IBI, and EDA). In other words, comparing the performance of our models by iteratively enriching the feature set enabled us to determine the relative impact these various sources of information have on aggression prediction accuracy.

Results

Data Collected

After a brief desensitization protocol involving increasing exposure to the wrist-worn biosensor, all 20 participants tolerated wearing the E4 and usable data were obtained in all cases (Table 2). Sixty-nine independent naturalistic observational sessions totaling 87 hr were collected (M = 4.35 hr, SD = 4.8 hr per participant). Within this corpus, a total of 548 aggressive episodes (M = 27, SD = 34 per participant) lasting an average duration of 28 sec (SD = 32 sec) were observed with concurrently collected E4 data.

Table 2. Naturalistic Data Collection Descriptive Statistics

Participant	PI	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17	P18	P19	P20	Group	Mean	*SD*
Number of sessions	5	3	3	2	2	2	8	9	2	1	1	1	2	6	1	1	10	1	5	4	69	3.45	2.84
Total Obs. duration[a]	9.33	3.97	3.77	3.02	1.25	0.57	7.02	8.47	2.72	1.43	0.22	1.38	1.6	8.47	0.52	1.02	20.48	0.78	5.1	5.87	86.99	4.35	4.80
Number of aggression episodes	72	7	13	8	9	6	35	30	50	1	2	3	9	39	1	8	130	2	76	47	548	27.40	33.84
Mean Agg. duration[b]	9	102	77	11	19	9	19	18	50	3	1	15	19	6	51	7	103	4	7	22	–	27.6	31.93

[a]Total observation durations are presented in hours.
[b]Mean aggression durations are presented in seconds.

Inter-rater reliability analysis on data randomly selected from 20% of our corpus of observed aggression onsets and offsets between two research staff from the inpatient site yielded 90% agreement and a corresponding Cohen's kappa of 0.79. A tolerance of 2 sec onset or offset difference between raters was considered an agreement. The average duration of observed aggression episodes was 28 sec, much longer than a potential absolute 4 sec difference between raters (Table 2).

Prediction Performance

Aggression prediction was performed using both global and person-dependent models, wherein data were processed every 15 sec for decision making. In global models, a single classifier was trained over a dataset containing time series across all sessions and all participants. In person-dependent models, individual classifiers were trained over time series within sessions from a single participant. In both models, 3 min of prior data ($\tau_p = 180$ sec) were used to make predictions in an upcoming time range (τ_f) since it accommodated the shortest individual observational session in our corpus.

Global prediction. The highest accuracy achieved in the global model used all extracted features from the past 3 min to predict aggression in the upcoming 1 min, with an AUC of 0.71 (represented by the solid ROC curve with 90% CI in Fig. 1).

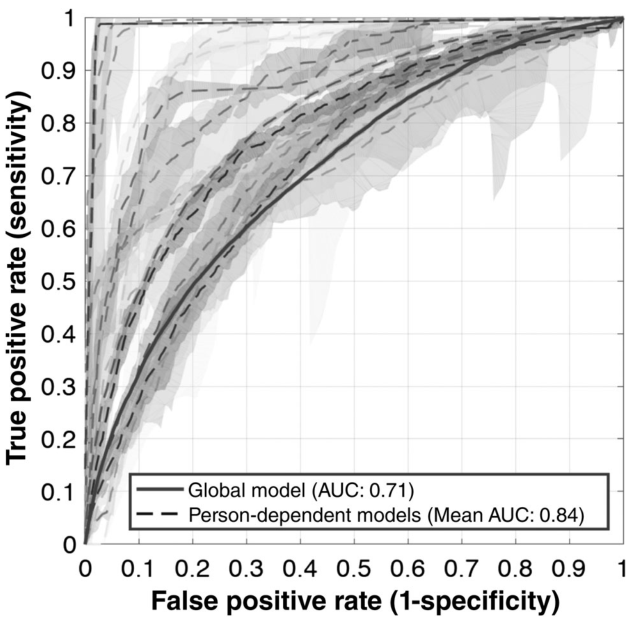

Figure 1. ROC curves with 90% confidence intervals to predict onset of aggression in the upcoming minute, using all features from the past three minutes. The solid line represents the global model, and each curve with dashed lines represents one of the person-dependent models.

Person-dependent prediction. Repeating the above analysis in person-dependent models (dashed lines in Fig. 1, rows in Table 3) produced an average AUC of 0.84 (min = 0.69, max = 0.99, *SD* = 0.10, 90% CI) predicting aggression in the upcoming 1 min using all extracted features from the past 3 min.

Comparative model performance. Person-dependent models produced a 0.13 average increase in AUC compared to the global model. Moreover, as seen in Figure 1, person-dependent models displayed more favorable sensitivity compared to the global prediction model.

Classifier performance and feature (signal) contributions. As seen in Table 3, models that included physiological and motion activity features outperformed those with only temporal features (AOF, TPA) across all participants, suggesting that biosensor data contribute unique information in the aggression prediction domain. Furthermore, Figure 2 indicates that when individual physiological features (EDA, BVP, and IBI) are systematically removed, no signal alone results in significant model fit change, that is, all individual physiological feature contributions are within the 90% CI.

Classifier performance and data properties. Correlations between model fit and total time observed, number of aggression episodes, and duration of observed aggression episodes were analyzed with Spearman's rho since these variables were skewed due to oversampling in some participants (D'Agostino and Pearson normality test, largest $P = 0.0067$). As seen in Figure 2, average time observed (M = 4.35 hr, SD = 4.8 hr) and number of observed aggressive episodes ($M = 27$, $SD = 34$) were both strong negative predictors of model fit/AUC, whereas duration of observed aggression episode (M = 28 sec, SD = 32 sec) was not. This suggests that the amount of data available to the model has a greater impact on prediction performance than duration of observed aggression episodes.

Discussion

Our findings demonstrate that a wearable biosensor and the data it generates may have promise in regard to predicting aggressive behavior in children with ASD. While other researchers have incorporated physiological data into studies of problem behaviors involving youth with ASD [Barrera, Violo, & Graver, 2007; Freeman, Grzymala-Busse, Riffel, & Schroeder, 2001; Freeman, Horner, & Reichle, 1999; Kushki, Khan, Brian, & Anagnostou, 2015; Lydon, Healy, & Dwyer, 2013; Nuske et al., 2018], prior work in this area has relied on artificial experimental settings and tasks, evaluated very brief time

Table 3. Mean AUC Values in Person-dependent Models Predicting Aggression Onset in the Next Minute Using Accumulated Data from the Past 3 min

Features	P1	P2	P3	P4	P5	P6	P7	P8	P9	P10	P11	P12	P13	P14	P15	P16	P17	P18	P19	P20	Mean	*SD*
Temporal	0.67	0.57	0.58	0.52	0.83	0.58	0.62	0.58	0.83	0.83	0.82	0.61	0.64	0.59	0.92	0.83	0.65	0.99	0.53	0.61	0.69	0.14
Motion	0.66	0.84	0.80	0.49	0.88	0.73	0.65	0.79	0.79	0.98	0.51	0.85	0.79	0.64	0.81	0.73	0.72	0.99	0.60	0.75	0.75	0.13
Physiological and motion	0.64	0.85	0.79	0.68	0.99	0.68	0.66	0.70	0.88	0.97	0.78	0.82	0.79	0.70	0.97	0.70	0.75	0.99	0.69	0.74	0.79	0.12
Physiological	0.71	0.86	0.81	0.67	0.98	0.75	0.68	0.76	0.88	0.99	0.83	0.87	0.85	0.71	0.99	0.72	0.78	0.99	0.70	0.78	0.82	0.11
All features combined	0.74	0.87	0.81	0.69	0.98	0.77	0.69	0.77	0.92	0.99	0.86	0.85	0.91	0.73	0.99	0.89	0.80	0.99	0.71	0.78	0.84	0.10

samples, or was correlational. Demonstrating that aggression can be predicted in the upcoming minute in an ecologically valid inpatient setting with 84% average accuracy is of potentially high clinical value. While we expect to increase prediction time as more data become available, focus groups we have conducted with parents and providers suggest that even 60 sec of warning may be a sufficient amount of time to triage attention, rearrange the environment to make it safer, provide redirection, calm the individual directly, or promote other self-management supports to decrease the risk of progression to dangerous aggression.

Our initial focus on aggression in more severely affected youth with ASD addresses critical gaps in the literature. Despite their apparent increased vulnerability to developing serious problem behaviors (Kanne & Mazurek, 2011), those more severely affected by ASD are underrepresented in intervention research [Stedman, Taylor, Erard, Peura, & Siegel, 2018]. Furthermore, it is common for this subpopulation to require high levels of intensive intervention (e.g., specialized school placements, psychopharmacology, and in-home behavioral therapies), which often exceed what providers in community settings can offer [Joshi et al., 2010; Siegel et al., 2012]. It can also land individuals with ASD in emergency rooms that are ill-equipped to handle them [Hoffmann, Stack, Monuteaux, Levin, & Lee, 2018] and necessitate costly psychiatric hospital care [Croen, Najjar, Ray, Lotspeich, & Bernal, 2006; Nayfack et al., 2014; Siegel & Gabriels, 2014]. Our use of an inpatient psychiatric population not only allowed us to enroll youth functioning poorly across domains who are underrepresented in research, but also provided a unique opportunity to study naturally unfolding aggression in a safe environment. It is also notable that the biosensor was well tolerated and produced analyzable signal data in a severely affected and primarily minimally verbal ASD sample.

The advantages of biologically based tools to identify processes that underlie behavioral dysregulation as it unfolds during moments of escalation are numerous and have great translational potential, especially for those unable to provide reliable self-reports on their arousal states. Our findings lay the groundwork for both expanding data collection on precursor behaviors associated with aggression [Borrero & Borrero, 2008; Hagopian, Rooker, & Yenokyan, 2018; Herscovitch, Roscoe, Libby, Bourret, & Ahearn, 2009] and future development of just-in-time adaptive intervention [Nahum-Shani et al., 2018] mobile health systems (mHealth) [Kumar et al., 2013] that may enable new opportunities for intervention before distress escalates to aggression. With input from parents and providers, a mobile application could be developed that displays real-time information on the risk for imminent aggression and prompts users to initiate de-escalation or emotion regulation interventions before

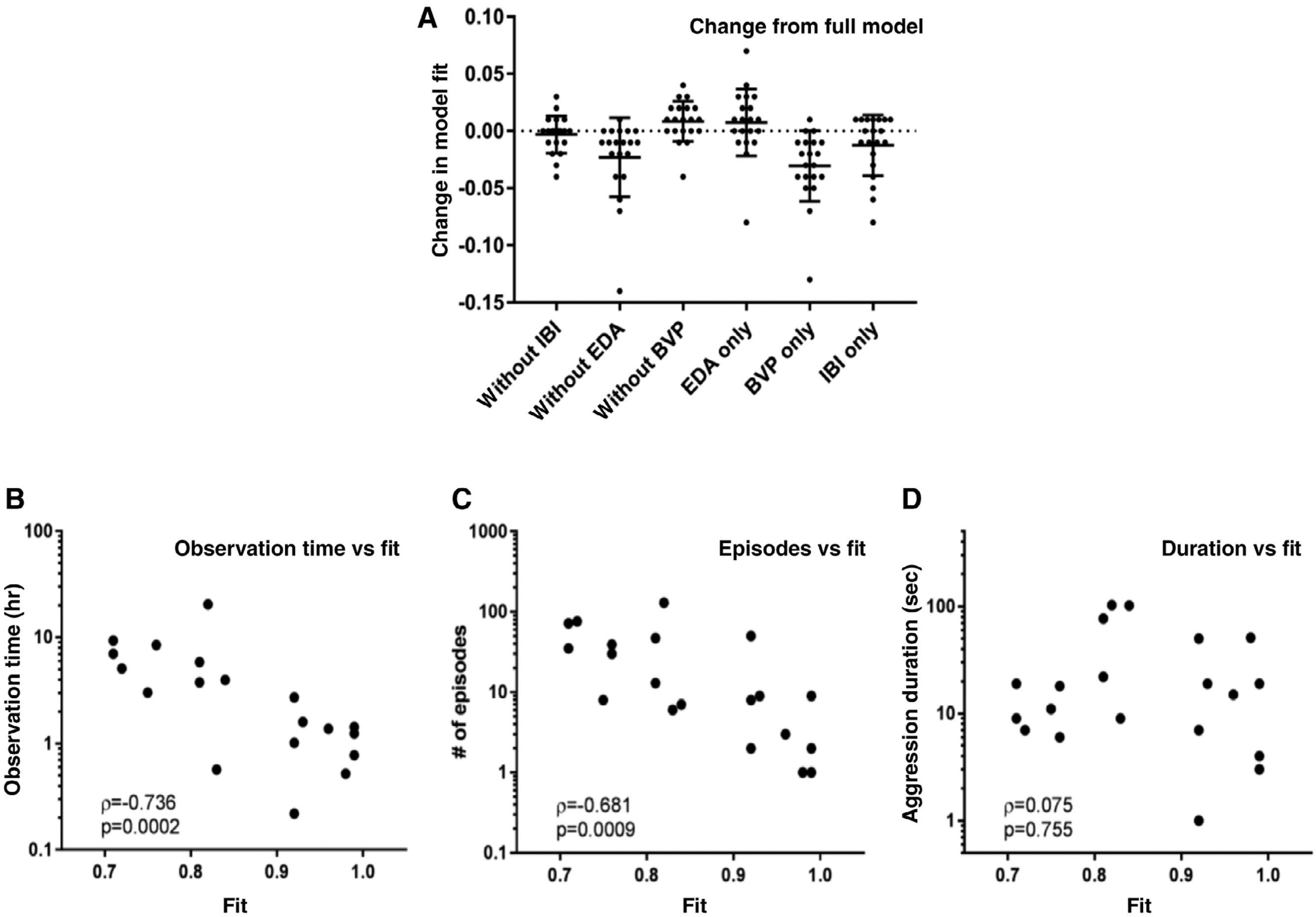

Figure 2. Individual physiological feature contributions to global model fit with 90% confidence intervals (A) and relationships between global model fit and behavioral observation time (B), number of aggressive episodes observed (C), and aggression duration (D).

it occurs [e.g., Alam, Anderson, Bankole, & Lach, 2018]. The effectiveness of such a system could be evaluated in its own right (i.e., directly comparing a behavioral and biosensor trial within the same study) as well as in combination with state-of-the-art pharmacological and behavioral treatment models [Conner et al., 2018; Frazier et al., 2010] to see if it further enhances aggression reduction. Uncovering physiological profiles relating to aggression in naturalistic settings may also enhance clinical trials research and precision medicine [Insel, 2014] by producing digital biomarkers [Adams et al., 2017] that better define psychiatric endophenotypes, enable recruitment of more targeted experimental groups, and help determine whether pharmaceuticals simply act as a sedative versus affect specific mechanisms that reduce physiological arousal associated with aggression. Finally, while our focus in this study was aggression to others, our methods could be applied to other prevalent problem behaviors in ASD (self-injury, property destruction, elopement, etc.), the wider outpatient ASD population, youth with other developmental disorders, as well as other populations who exhibit frequent aggression.

While we obtained good predictive performance in the current study, the design of our machine learning models reduced opportunities for cross-training along different time windows (i.e., using data from one window for another window) and may have led to overfitting (i.e., models are overparameterized). In future work, we will institute a generative nonhomogeneous Poisson process model that introduces a common prior probability across windows to enable cross-learning and avoid overfitting. This approach may allow us to generate more optimal prediction performance by learning sparse linear models that identify which features correlate most strongly with aggression onsets. We also plan to address the potential issue of data quality and nonstationarity in physiological signals by extracting features that achieve immediate generalization across time. Moreover, we will explore insensitivity and modern transfer learning techniques that can be quickly adapted to changing conditions through online adaptation with limited training data in a new setting (i.e., new day for the same individual, a new individual, etc.), and assess hybrid classifiers wherein the most significant features from global and person-dependent models are combined to increase computational efficiency (i.e., start with the global features most strongly associated with high prediction accuracy and update with person-dependent features). Finally, we will work to reduce false positive and false negative predictions through feature optimization; however, as communicated to us by inpatient clinical staff, the potential benefit of avoiding or reducing a dangerous aggressive event is likely to outweigh potential harm associated with false positives in clinical practice.

Our results suggest that the person-dependent models were more accurate than the global model, and we observed individual differences in prediction accuracy (i.e., 30% difference between highest and lowest prediction performance, Table 3). However, a limitation of this study is the nonuniform frequency and duration of observed aggression across participants (evidenced in Table 2), making it difficult to determine the relative impact the amount of training data has on model prediction performance. Larger trials are needed to further establish an ideal ratio of measurement density to predictive accuracy and reliability. Also, considering the moderating influences emotion dysregulation and language ability/communication efficiency can have on aggression [Berthoz & Hill, 2005; Costa, Steffgen, & Samson, 2017; Mazefsky et al., 2013; Mazefsky & White, 2014; Samson, Hardan, Lee, Phillips, & Gross, 2015], we expect that a proportion of the person-dependent variability we observed might be explained by emotion regulation and verbal ability. In an extension of this work that we are now beginning, we will gather this information and evaluate whether it improves model prediction performance. We have also begun to explore the relationship between observable affect, internal physiology, and subsequent aggression to determine if it is concordant or discordant in individuals with ASD. Finally, we plan to include a broader sample of both verbal and minimally verbal youth with ASD in order to assess the generalizability of our results.

Conclusion

This study sought to define a more generalized, objective, and biological approach to understanding and predicting aggression in ASD, grounded in underlying physiological mechanisms, with a severely affected population who suffer some of the greatest morbidity but have received relatively little attention. In so doing, we seek to develop a different and potentially additive approach to traditional attempts that differentiate proactive or reactive aggression, focus on the potential function(s) of a behavior, or utilize psychopharmacology. Our results suggest that cutting-edge technology combined with multidisciplinary clinical experience has the potential to further inform what has been a largely intractable problem for a sizable segment of the ASD population, who are arguably most in need of innovative approaches. By focusing on reducing the unpredictability of aggression, we hope that the knowledge, data, and algorithms generated in this ongoing program of research could ultimately facilitate reductions in the occurrence, duration, and impact of aggression in youth with ASD, enabling them to more fully participate in their homes, schools, and communities.

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