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Brief Report: Machine Learning for Estimating Prognosis of Children with Autism Receiving Early Behavioral Intervention – A Proof of Concept

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Abstract

Even when an intervention has empirical support in the research literature, some children with autism make more progress than others. Hence, researchers should develop solutions to identify children most likely to benefit from a given intervention. One potential solution is to use machine learning to guide these predictions. To address this issue, our study compared five machine learning algorithms in estimating treatment prognosis on adaptive functioning and autistic symptoms in children with autism receiving early behavioral intervention. Each machine learning algorithm produced better predictions than random sampling on both outcomes. Those results indicate that machine learning is a promising approach to estimating prognosis in children with autism, but studies comparing these predictions with those produced by qualified practitioners remain necessary.

Keywords: autism, differential response, early behavioral intervention, machine learning, prognosis

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One challenge faced by practitioners who intervene with individuals with mental health and developmental disorders involves estimating prognosis given a specific treatment (Cearns et al., 2019; Dwyer et al., 2018). One potential solution to this problem is to use machine learning to develop models that could predict prognosis. Machine learning is a subdomain of artificial intelligence that involves using algorithms to "train" a model to recognize patterns in data in order to make predictions (Turgeon & Lanovaz, 2020). Concretely, the experimenter provides data (pre-intervention data and outcomes) from prior clinical or research cases to the algorithm, which attempts to predict the outcomes using the pre-intervention data. Once the model has been trained, it is tested for generalization on novel cases (not used to train it). Several different algorithms for machine learning exist to train models such as logistic regression, *k*-nearest neighbors, gaussian process, random forests, and support vector machines (see Singh et al., 2016, for review). Each of these algorithms transforms the data in a different manner, which makes it difficult to predict a priori which one will produce the most accurate results. Another challenge involves the type of data provided to the algorithm (Parikh et al., 2019). When training the model, should experimenters provide overall scores (e.g., global IQ) or individual scales (e.g., verbal IQ)?

To address these issues, the purpose of our exploratory study was to apply different algorithms to examine whether they could predict the effects of a treatment for autism by using global and specific measures. As we had access to a large dataset of children receiving early behavioral intervention, we chose to examine whether we could predict the response of children with autism to this intervention. Despite showing positive effects on adaptive functioning and autistic symptoms (Eikeseth et al, 2012; Reichow et al., 2018), the results of early intervention outcome studies consistently report differential response to intervention across children (Fava & Strauss, 2014; Howlin et al., 2009; Magiati et al., 2011; Makrygianni et al., 2018; Reichow et al., 2018). Heterogeneity in outcomes remains poorly understood; to date, researchers have yet to identify highly reliable predictors of early behavioral intervention outcomes (Eapen et al., 2013; Eldevik et al., 2010; Reichow, 2012; Smith et al., 2015; Warren et al., 2011). Due to the heterogeneity of autism, determining who will benefit most from treatment is an important question (Tiura et al., 2017). Given the challenges associated with estimating prognosis for children with autism receiving early intervention, comparing the relative prediction accuracy of different algorithms regarding improvement on adaptive functioning and autistic symptoms may eventually prove useful to practitioners.

Method

Participants

Our dataset originates from a study assessing the effects of a community-based intervention program conducted with 233 unselected children from 2009 to 2012 (see Préfontaine et al., 2021). Children received either a low-intensity intervention (i.e., between 4 and 12 hours weekly) or a moderate-intensity intervention (i.e., between 16 and 20 hours weekly) based on the principles of applied behavior analysis, which qualified as early behavioral intervention[1] in our province (Quebec, Canada). The program was mostly based on the work of Lovaas and Maurice (Lovaas, 1981; Maurice & et al., 1996) and adopted a 1:1 child-to-technician ratio. The intensity option was determined using a needs assessment conducted at enrollment, and the preferences and availability of the parents (see Rivard et al., 2014, 2019 for more details about the intervention). Participants were aged between 2.50 to 5.75 years old (*M* = 4.34, *SD* = 0.47) at the

[1] Because the intensity of the intervention provided to our sample may not qualify the intervention as being "intensive", we will use the expression early behavioral intervention when referring to the program.

start of the program and received a diagnosis of ASD from an independent multidisciplinary team. Parents provided written consent for their child prior their participation in the study. The original project (see Rivard et al., 2014; 2019) used a prospective longitudinal design with annual assessments. We used the data from time 1 (representing baseline) and time 2 (representing post-intervention 12 months after baseline) to train and test the machine learning algorithms to estimate the prognosis of short-term outcomes. Our analyses involved two subsamples for which we had complete data for the outcome variables (i.e., adaptive functioning, n = 216; autistic symptoms, n = 149). Some children are in both subsamples (n = 147) because we had complete data for the two outcome variables. The adaptative functioning model and the autistic symptoms model were developed separately. Table 1 presents the descriptive statistics for each sample.

Machine Learning

Machine learning algorithms involve training a model to recognize patterns in data to make predictions (Turgeon & Lanovaz, 2020). Two types of data are required for supervised learning: features and labels. Features are the input data that the algorithms use to make predictions. The features represent measurable aspects of the studied phenomenon. Labels are the output data, or the results of the prediction. The algorithm trains a model to recognize the patterns between features and labels in a subsample (i.e., training set) to make predictions on the remaining subsample (i.e., test set).

Features

We used individual characteristics that are considered potential predictors of early behavioral intervention effectiveness as features: age at enrollment (Bieleninik et al., 2017; Makrygianni & Reed, 2010), intellectual functioning (Makrygianni & Reed, 2010; Reed, 2016; Tiura et al., 2017), autistic symptoms (Flanagan et al., 2012; Reed, 2016), and adaptive functioning (Eldevik et al., 2010; Flanagan et al., 2012; Reed, 2016; Sallows & Graupner, 2005;

Vivanti et al., 2014). In addition, prior research has reported behavioral and cognitive differences across gender (Frazier et al., 2014; Hull et al., 2017), and some evidence has suggested that high socio-economic status is associated with better outcomes for the intervention (Gabriels et al., 2001; Magiati et al., 2011). Consequently, we also included gender and annual income among the features.

We briefly describe how each feature was measured below, but readers can consult Préfontaine et al. (2021) for more comprehensive descriptions. Age was a continuous variable, where decimals allowed to record the exact age of the participants (i.e., 2-year-old and 6-month-old was coded as 2.5). Research assistants supervised by a psychologist administered the *Wechsler Preschool and Primary Scale of Intelligence* (WPPSI-III; Wechsler, 2003) to measure intellectual functioning. A parent and a special education technician[2] completed the *Childhood Autism Rating Scale – Second Edition* (CARS-2; Scholper et Van Bourgondien, 2010). We used the average score between the two respondents because they were highly correlated (r = .81). A parent completed the *Adaptive Behavior Assessment System-II* (ABAS-II; Harrison and Oakland, 2003) to assess adaptive functioning. Gender of the participants was a dichotomous variable (code 1 = female and 2 = male). Annual family income was an ordered-categorical variable (code 1 = $10,000 to $29,999, 2 = $30,000 to $49,999, 3 = $50,000 to $69,999, 4 = $70,000 to $89,999, and 5 = Over $90,000) and was reported by the parent in Canadian dollars.

Labels

We used two labels: improvement of autistic symptoms and improvement in adaptive functioning. We chose those labels to represent response to intervention because a recent systematic review has observed reductions in autistic symptoms and improvements in adaptive

[2] Special education technicians is a terminology unique to the province of Quebec and refers to college-level technicians.

function as primary outcomes of early behavioral intervention (Reichow et al., 2018). For both variables, change scores were compute by subtracting the score at time 1 from the score at time 2. Then, we transformed the labels values to binary outcomes. For autistic symptoms, a change score of 0 or more represented no improvement, and a change score of lower than 0 represented improvement. For adaptive functioning, a change score of 0 or less represented no improvement and a change score higher than 0 represented improvement.

Algorithms

One of the important aspects when building a machine learning model is determining the appropriate algorithm for the task at hand (Yang & Shami, 2020). Different algorithms make predictions using the features in different ways. We compared the prediction of five algorithms that can solve classification problems (i.e., logistic regression, *k*-nearest neighbors, Gaussian process, random forest, and support vector classifier). Logistic regression is a linear model that identifies a cut-off (or threshold) to separate label values and produces a classification according to this cut-off (Yang & Shami, 2020). The *k*-nearest neighbors algorithm uses the *k* closest cases to identify the appropriate classification (Yang & Shami, 2020). That is, the training data are graphed in a multidimensional space according to their features and the algorithm categorizes novel test data by attributing them the classification of the majority of their *k* closest cases. Gaussian process consists of tracing the Gaussian curves for each feature and each label in the training set, and predicting the label for the test set according to the relative position of the novel data on the Gaussian curves (Daemi et al., 2019). The random forest algorithm involves building numerous decision trees to resolve classification problems (Jiang et al., 2020). Each tree in the forest makes a prediction, and this forest selects the classification supported by the largest number of trees. The support vector classifier projects the data in a higher dimension and then separates the classes using a hyperplane (Yang & Shami, 2020). Projecting the data into a higher dimension allows their separation in classes, solving the overlapping problem in the lower dimension.

Analyses

To limit the risk of overfitting and considering our small sample size, we used the *k*-fold cross-validation method (Yarkoni & Westfall, 2017) to train the models and test the accuracy of the prediction for each algorithm. The *k*-fold cross-validation method consists of randomly splitting the dataset in *k* groups (here, $k = 5$); the first group is treated as the test set and the model is trained on the remaining groups. The procedure is repeated *k* times, so that each group forms the test set once. In this context, accuracy represents the average percentage of agreement (i.e., number of agreements divided by total of participants) between the true values and the predicted labels for each fold. To be able to qualify the performance of the different algorithm, we also computed the accuracy of random sampling for the two labels over 10,000 iterations.

We conducted the analyses individually for the two outcome variables (i.e., adaptive functioning and the autistic symptoms). We trained and tested a total of 20 models (10 for adaptive functioning and 10 for autistic symptoms). For the two models, we tested the five described algorithms, and for each algorithm, we conducted the analyses twice with two different sets of features to identify which one predicted improvement best. The first set contained gender, age, family annual income, autistic symptoms, full-scale IQ and general adaptive functioning score. The second set contained gender, age, family annual income, autistic symptoms, the three scales of IQ (namely, verbal IQ, performance IQ and general language composite score) and the three domains of adaptive functioning (namely, the conceptual, social and practical domains). We chose to test these two sets to examine whether having more precise features (i.e., scales vs. global scores) would lead to more accurate predictions.

Results and Discussion

Table 2 presents the accuracy for each algorithm on the test set. The upper panel shows the results for the first set of features (global) and the lower panel shows the results for the second set of features (scales). For both sets of features, the machine learning algorithms produced better predictions than random sampling. The mean difference between the random sampling and the predictions of the algorithms was 11.2% for adaptive functioning and 6.5% for autistic symptoms. Comparing the two sets of features, the prediction accuracy for the same algorithm was similar, with an average difference of 1.4% for adaptive functioning and 1.7% for autistics symptoms. This result indicates that the predictions were similar regardless of whether we used the full-scale scores (i.e., full-scale IQ and the general adaptive composite score) or the scale scores (i.e., the verbal IQ, performance IQ and global language composite scores, and the conceptual, social and practical domains of adaptive functioning) as input. In both sets, the algorithms predicted adaptive functioning with better accuracy than autistic symptoms. Comparing algorithms with each other, the Gaussian process performed best on adaptive functioning, and the support vector classifier achieved the most accurate predictions for autistic symptoms. None of the algorithms produced systematically worst predictions than all the others.

Our results are consistent with previous work that used machine learning to predict treatment outcomes in depression (Chekroud et al., 2016). Their machine learning models produced predictions with an accuracy ranging from 59.6% to 64.6%, while clinicians had an average accuracy of 49.3%. In the same vein, the next important step in this line of work would be to assess whether the algorithms can estimate prognosis better than qualified practitioners who intervene with children with autism. To this end, machine learning should not aim for absolute (or perfect) accuracy, but rather demonstrate its incremental utility by improving on current practices (Cearns et al., 2019). Improving the estimation of prognosis would allow practitioners to adjust their intervention when a child is not showing the expected progress.

Our study has some limitations that should be noted. The small sample size limited the cross-validation techniques that we could use and probably had an impact on accuracy. To address this issue, future research should replicate our study with larger sample sizes. A larger sample size would also allow researchers to tune the hyperparameters in order to optimize (i.e., improve) the models. Overlooking hyperparameters tuning is a frequent limitation in current machine learning work in psychiatry, and tuning hyperparameters may help discriminate between algorithms by improving their prediction accuracy in a differential manner (Cearns et al., 2019). Finally, an interesting avenue for future research would be to diversify the features used, as machine learning has the capacity to integrate a large amount of data from different sources (e.g., behavioral, genetic, neuroimaging) in the same model (Miotto et al., 2018; Sengupta et Shrestha, 2019; Shatte et al., 2020). This interdisciplinary approach has the potential to further improve the accuracy of models used to predict response to intervention, by including genetic and other biological variables, in addition to relevant psychological (e.g., IQ) and socioeconomic (e.g., family income) variables.

Compliance with Ethical Standards

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Ethical Approval: All procedures performed in this study were in accordance with the ethical standards of the Canadian Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans and with the 1964 Helsinki declaration and its later amendments.

Informed Consent: Parents provided informed consent for them and their child.

Conflict of Interest: The authors have no conflict of interest to report.

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Table 1

Descriptive Statistics of Each Subsample

Characteristics	Adaptive functioning subsample (*n* = 216) Time 1 *M (SD)*	Adaptive functioning subsample (*n* = 216) Time 2 *M (SD)*	Autistic symptoms subsample (*n* = 149) Time 1 *M (SD)*	Autistic symptoms subsample (*n* = 149) Time 2 *M (SD)*
Age	4.32 (0.47)	-	4.26 (0.44)	-
Full-scale IQ	70.85 (20.17)	-	70.94 (19.30)	-
Verbal IQ	72.12 (17.26)	-	71.43 (16.04)	-
Performance IQ	79.59 (20.49)	-	80.44 (20.43)	-
General language composite	73.73 (19.46)	-	73.57 (18.62)	-
Autistic symptoms	31.61 (7.70)	29.63 (7.45)	31.66 (7.35)	29.50 (7.46)
General adaptive functioning	64.14 (14.08)	72.89 (17.48)	63.96 (14.14)	73.04 (16.92)
Conceptual domain	67.77 (14.52)	74.81 (17.34)	67.65 (14.80)	75.08 (17.18)
Social domain	69.74 (15.99)	75.88 (18.70)	69.49 (15.99)	75.94 (18.27)
Practical domain	64.89 (13.70)	67.99 (16.39)	64.87 (13.68)	68.11 (15.32)
	N	%	*N*	%
Gender				
Male	171	79.17	122	81.88
Female	45	20.83	27	18.12
Annual income				
$10,000 to $29,999	44	20.37	29	19.46
$30,000 to $49,999	50	23.15	38	25.50
$50,000 to $69,999	41	18.98	31	20.81
$70,000 to $89,999	32	14.81	24	16.11
Over $90,000	43	19.90	24	16.11

Table 2

Average Prediction Accuracy of Each Algorithm on the Test Set

	Random Sampling	**Logistic Regression**	***k* Nearest Neighbors**	**Gaussian Process**	**Random Forest**	**Support Vector Classifier**
First set of features (using full-scale scores)						
Adaptive Functioning	.542	.639	.648	.684	.662	.662
Autistic Symptoms	.545	.631	.603	.610	.597	.638
Second set of features (using scales scores)						
Adaptive Functioning	.542	.648	.625	.671	.648	.653
Autistic Symptoms	.545	.598	.583	.591	.611	.638