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Ados module 3 sample report

Searching for a minimal set of behaviors for autism detection through feature selection-based machine learning Your article has downloaded Charlotte K pper, Sanna Stroth, ... Stefan Roecke Nicole Wolff, Gregor Kohls, ... Veit Roessner Halim Abbas, Ford Garberson, ... Dennis P. Wall Suma Jacob, Jason J. Wolff, ... Jed T. Elison Wail M. Hassan, Abeer Al-Dbass, ... Afaf El-Ansary Jonathan T. Megerian, Sangeeta Dey, ... Sharief Taraman Laurent Mottron & Danilo Bzdok J r my Lefort-Besnard, Kai Vogeley, ... Danilo Bzdok Bokan Bao, Javad Zahiri, ... Eric Courchesne Although the prevalence of autism spectrum disorder (ASD) has risen sharply in the last few years reaching 1 in 68, the average age of diagnosis in the United States remains close to 4—well past the developmental window when early intervention has the largest gains. This emphasizes the importance of developing accurate methods to detect risk faster than the current standards of care. In the present study, we used machine learning to evaluate one of the best and most widely used instruments for clinical assessment of ASD, the Autism Diagnostic Observation Schedule (ADOS) to test whether only a subset of behaviors can differentiate between children on and off the autism spectrum.

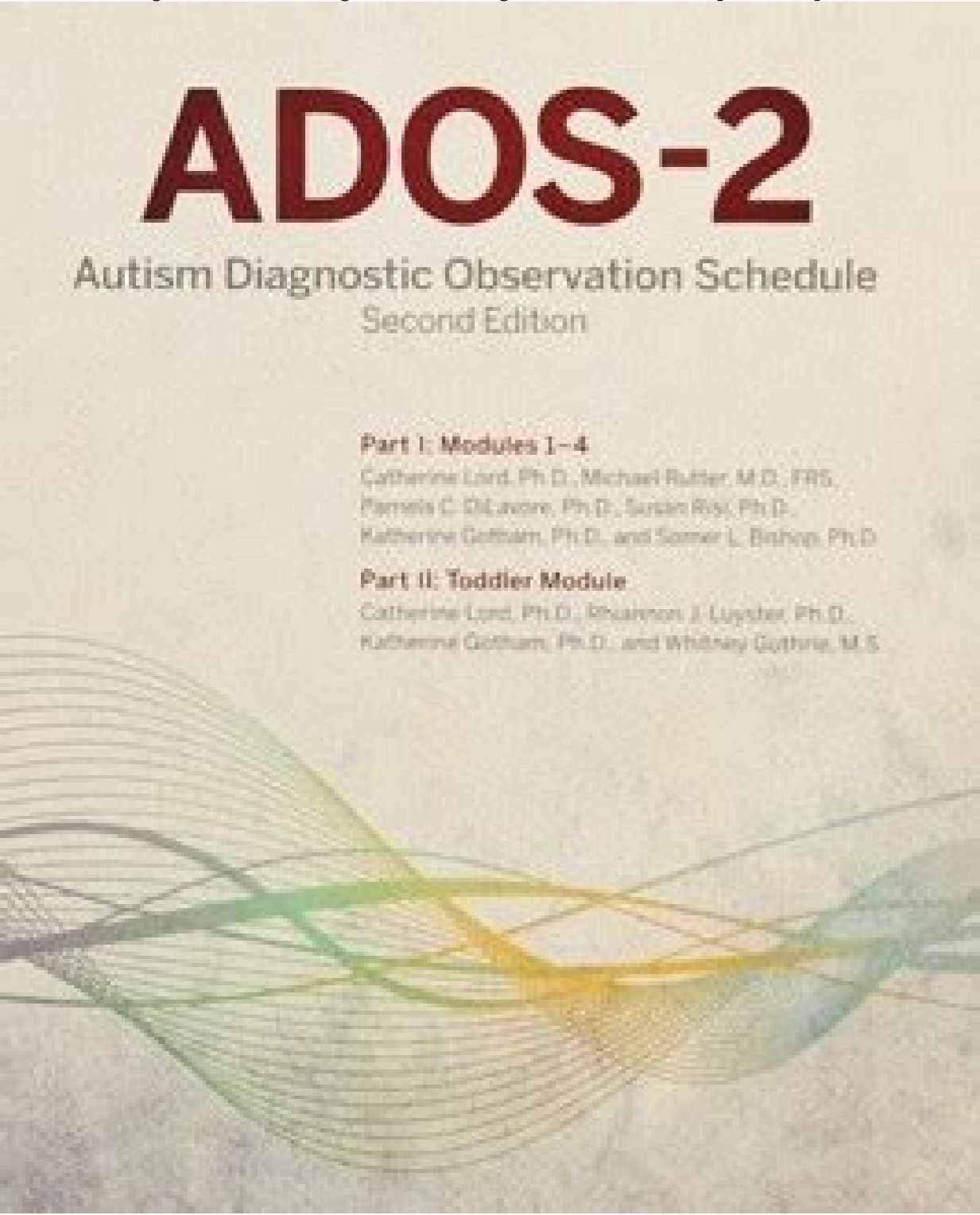
Study group	Baseline ADOS module (rows)	Evaluation ADOS module (columns)				Module changes <sup>a</sup>				Odds ratio for any change of module: intervention vs. comparison group <sup>b</sup>			
		Total				Positive change		No change		Crude OR	Adjusted <sup>c</sup> OR [95% CI]		
			1	2	3	n	%	n	%				
Intervention group	1	44	18	13	13	39	58.2	28	41.8	1.2, <i>p</i> = .7	2.0 [0.7, 6.0], <i>p</i> = .2		
	2	23	0	10	13								
	3	0	0	0	0								
Comparison group	1	9	5	2	2	14	53.8	12	46.2				
	2	17	0	7	10								
	3	1	0	0	1								

Note. ADOS = Autism Diagnostic Observation Schedule. Odds ratios (OR) were obtained using univariate and multivariable logistic regression analyses.  
<sup>a</sup>Presence of ADOS module used as baseline and as evaluation. <sup>b</sup>Adjusted for developmental delay and ADOS module as baseline. <sup>c</sup>After adjustment.

ADOS relies on behavioral observation in a clinical setting and consists of four modules, with module 2 reserved for individuals with some vocabulary and module 3 for higher levels of cognitive functioning. We ran eight machine learning algorithms using stepwise backward feature selection on score sheets from modules 2 and 3 from 4540 individuals. We found that 9 of the 28 behaviors captured by items from module 2, and 12 of the 28 behaviors captured by module 3 are sufficient to detect ASD risk with 98.27% and 97.66% accuracy, respectively. A greater than 55% reduction in the number of behavioral with negligible loss of accuracy across both modules suggests a role for computational and statistical methods to streamline ASD risk detection and screening. These results may help enable development of mobile and parent-directed methods for preliminary risk evaluation and/or clinical triage that reach a larger percentage of the population and help to lower the average age of detection and diagnosis. Rates of autism spectrum disorder (ASD) continue to climb, now impacting 1 in 68 individuals in the United States.1 Despite important progress in understanding the genetics of ASD,2, 3 ASD remains diagnosed through behavioral examination. The diagnosis of ASD is currently made using instruments designed to measure impairments in the two core domains of ASD, as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V): (1) communication and social interaction and (2) restricted interests and repetitive behaviors.



The Autism Diagnostic Observation Schedule (ADOS)<sup>4</sup> is one of the most widely used instruments to assist in ASD diagnosis. The ADOS consists of a series of semi-structured activities designed to elicit specific behaviors of social interaction, communication, imaginative use of objects, restricted interests and repetitive behaviors. The diagnostic test is split into four modules, each tailored to specific individuals based on their language and developmental level to ensure coverage of a diverse set of behavioral manifestations.<sup>4</sup> A certified professional at a clinical facility first administers the ADOS examination and then scores the individual based on his or her observations to determine the final diagnosis. The initial assessment can take between 30 and 60 minutes, and the scoring increases the total time to between 60 and 90 minutes. Due to variance in inter-rater reliability, additional professionals may re-score the individual, further increasing the time between testing and receipt of the official clinical diagnosis.<sup>4</sup>Even ignoring the geographic and logistical hurdles in finding a certified professional to administer the ADOS, the time required for the exam and the rise in the number of children at risk for ASD have contributed to increasing bottlenecks in the healthcare system.<sup>5</sup> The average age of diagnosis in the United States hovers stubbornly around 4 years,<sup>5</sup> and families may wait as long as 13 months for the diagnosis after the initial screening,<sup>6</sup> and even longer if they are from a minority population or are of lower socioeconomic status.<sup>7</sup> Such delays impede early intervention speech and behavioral therapies that provide substantial benefits to children.<sup>8, 9</sup> For the estimated 27% of individuals undiagnosed at 8 years of age,<sup>5</sup> opportunities for therapeutic intervention have dissipated. Therefore, risk assessment and triage tools that can reach families earlier and enable them to receive the care they need are badly needed.Given the promising findings from our previous work on the first module of the ADOS<sup>10, 11</sup> and the ADI-R,<sup>12</sup> we postulated that we might obtain similar results when examining records from the other two modules of the ADOS, which apply to a large portion of the population suspected of having an ASD.<sup>13</sup> Improving upon our previous work, here we utilized the best-estimate clinical diagnosis when possible and incorporated stepwise backward feature selection into our machine learning pipeline to quantitatively select the optimal set of significant behavioral features that can accurately detect ASD risk in a large population of individuals. We assembled a collection of ADOS evaluations for 4540 individuals and developed a classifier for each module that exhibited optimal performance in classification of individuals both on and off the spectrum. Each classifier was trained on over 600 individuals and tested independently on more than 1000 individuals. The resulting classifiers contained fewer items than the ADOS-2 (ref. 14) and pinpointed several behaviors that could help guide future efforts focused on expeditious observation-based screening both in and out of clinical settings.Data for modules 2 and 3 came from five separate repositories: Boston Autism Consortium (AC), Simons Simplex Collection v14 (SSC),<sup>15</sup> Autism Genetic Resource Exchange (AGRE),<sup>16</sup> National Database of Autism Research (NDAR)<sup>17</sup> and the Simons Variation in Individuals Project (SVIP)<sup>18</sup> (Table 1). The ADOS examination classified individuals into three discrete categories (autism, autism spectrum, and non-spectrum) by summing the scores from a subset of items from the ADOS and cross-referencing this total score with the thresholds for autism, autism spectrum and non-spectrum. ADOS scores for each item fall on an integer scale of 0–3, with scores of 7 or 8 reserved for behaviors not exhibited during the test. In a preprocessing step, the ADOS algorithm recodes scores of 3 to 2 and scores of 7 or 8 to 0 to improve reliability and validity.<sup>14</sup> For our analyses, we recoded scores of 7 and 8 as 0, but elected to leave scores of 2 and 3 as distinct answer codes to increase granularity in the classification. In addition, we grouped strict autism and autism spectrum categories together into one autism spectrum cohort, leaving only two classes for machine learning, an autism spectrum class and a non-spectrum class.Table 1 Training and testing data descriptionRecruitment varied by study. Individuals in AC, AGRE, NDAR and SSC were recruited with a suspicion of having ASD, and individuals in the SVIP were required to have or be related to an individual with the 16p11.2 duplication/deletion.<sup>19</sup> Gender remained consistent across both modules: males comprised 82–86% of individuals with ASD and 61–63% of individuals without ASD. The intelligence quotient (IQ) was consistent across both modules and between individuals with and without ASD (Table 2). Due to the diverse phenotypic effects of the 16p11.2 duplication/deletion, individuals in SVIP were enriched for comorbidities, including ADHD, developmental coordination disorder, phonological disorder and others. Thus, the individuals in the SVIP proved useful for testing the specificity of the algorithms (i.e., differentiating between ASD and other behavioral disorders and developmental delays). A complete description of the phenotypic diversity of the samples used is provided in Supplementary Table S1.Different versions of the ADOS were used in each data set, namely ADOS Version 1 (ref. 4) (AC, SSC, AGRE and NDAR), and ADOS version 2 (ref. 14) (SVIP). To ensure consistency across data sets, we computed the ADOS-2 diagnosis for all individuals in AC, AGRE, NDAR and SSC using the ADOS-2 algorithms. We elected to do this because the ADOS-2 incorporates repetitive and restrictive behaviors, and it has been shown to more accurately identify cases from non-spectrum controls in lower-functioning populations.<sup>14</sup> Not all individuals had either a clinician's diagnosis or the best-estimate clinical diagnosis. Specifically, 76% of the ASD cases and 46% of the non-autism controls had a recorded clinician's diagnosis or the best-estimate clinical diagnosis. Therefore, we elected to use the diagnosis provided by the ADOS-2 algorithm for our classifier labels in the training processes.Table 2 Sample descriptionMachine learningWe used machine learning to develop two classifiers: one derived from ADOS module 2 and the other from ADOS module 3. For each module, our strategy involved training eight different machine learning algorithms (Table 3) using stepwise backward feature selection, and testing the final classifier on four independent data sets. We chose stepwise backward feature selection over stepwise forward feature selection to allow for interactions between features.<sup>20</sup> We used each module's items as features, and the individuals' ADOS-2 diagnoses as our prediction class. All machine learning analyses were performed in R and Weka21 (version 3.7-9). As the number of individuals with ASD outnumbered those without in both module 2 (~4:1) and module 3 (~5:1) across all data sets, we selected the data set with the highest number of individuals without ASD as our training set. Module 2 classifiers were trained from an NDAR collection of 362 with ASD and 282 individuals without ASD. Module 3 classifiers were trained on AGRE, with 510 individuals with ASD and 93 individuals without ASD (Table 1).Table 3 Machine learning algorithms used in trainingThe 28 features for each of module 2 and module 3 were ranked using a support vector machine (SVM) based on their ability to differentiate between individuals with and without ASD. We used stepwise backward feature selection with 10-fold cross-validation in all eight machine learning algorithms. This feature selection procedure determined the optimal number of features by first training a classifier with all 28 features, iteratively removing the lowest-ranked feature, and building a new model using 90% of the data for training and the remaining 10% for testing. cour de mathematique 5eme pdf



The process ended once a single feature remained, yielding a final set of 28 classifiers, which could each be assessed for their sensitivity and specificity. By plotting the sensitivity, specificity and accuracy of each classifier versus the number of features, the best classifier was identified as the one with the highest performance and smallest number of features (Figure 1). We aimed to maximize specificity (the true negative rate) over sensitivity (the true positive rate) because of the large class imbalance (Table 1).Figure 1Module 2 logistic regression and logistic model tree (LMT) training results. Sensitivity and specificity of the module 2 logistic regression and LMT classifiers based on the number of features used during training on the National Database of Autism Research are provided in Table 1. The nine-feature logistic regression classifier (blue dot) was used in testing.ValidationAfter finding the optimal classifiers for modules 2 and 3, we validated these classifiers on the remaining four data sets not used for training. The module 2 classifier was tested on AC, AGRE, SSC and SVIP, totaling 1089 individuals with ASD and 66 individuals without ASD (Table 1). The module 3 classifier was tested on AC, NDAR, SSC and SVIP, totaling 1924 individuals with ASD and 214 individuals without ASD (Table 1).Two algorithms using the same nine features displayed optimal performance on the NDAR training data (98.90% sensitivity, 98.58% specificity and 98.76% accuracy), a logistic regression<sup>22</sup> and a logistic model tree (LMT)<sup>23</sup> (Table 3; Figure 1). atomic habits worksheets LMTs combine decision trees with logistic regression, thereby allowing the incorporation of nonlinear patterns into the model. When such nonlinear patterns exist and help explain additional variance in the data, LMTs outperform logistic regression.<sup>23</sup> However, in our data, no such patterns were detected and the nine-feature LMT consisted of just the root node with a logistic regression model. Thus we chose logistic regression over LMT for use in further testing and validation.For independent validation of the nine-feature logistic regression classifier, we collated score sheets for module 2 from the AC, AGRE, SSC and SVIP (Table 1) to determine whether the classifier could recapitulate the sensitivity and specificity of training data on held-out test data.

