Autism Spectrum Disorder Screening: Machine Learning Adaptation and DSM-5 Fulfillment

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ABSTRACT

One of the primary psychiatric disorders is Autistic Spectrum Disorder (ASD). ASD is a mental disorder that limits the use of linguistic, communicative, cognitive, skills as well as social skills and abilities. Recently, ASD has been studied in the behavioural sciences using intelligent methods based around machine learning to speed up the screening time or to improve sensitivity, specificity or accuracy of the diagnosis process. Machine learning considers the ASD diagnosis problem as a classification task in which predictive models are built based on historical cases and controls. These models are supposed to be plugged into a screening tool to accomplish one or more of the aforementioned goals. In this paper, we shed light on recent studies that employ machine learning in ASD classification in order to discuss their pros and cons. Moreover, we highlight a noticeable problem associated with current ASD screening tools; the reliability of these tools using the DSM-IV rather than the DSM-5 manual. Hence the necessity to amend current screening tools to reflect the new imposed criteria of ASD classification in the DSM-5 particularly the diagnostic algorithms embedded within these methods.

CCS Concepts

•Theory of computation → Models of learning •Computing methodologies → Supervised learning •Information systems → Clustering

Keywords

Accuracy; Autism Spectrum Disorder-ASD; ADOS; ADI; Classification; DSM-5; Predictive Models; Machine Learning

1. INTRODUCTION

ASD is considered a brain development disorder that limits certain communication and social behaviours [7]. There have been a number of diagnosis tools for ASD. Examples of clinical diagnosis methods are Autism Diagnostic Observation Schedule-Revised (ADOS-R) [14], Autism Diagnostic Interview (ADI) [15], and many others. The clinical diagnostic methods have showed competitive performance in screening cases related to ASD. For instance, ADOS-R and ADI have derived good sensitivity and specificity results in several different experimental research studies, i.e. for example, [2]; [18]; [23]. Furthermore, both methods have revealed acceptable to high reliability and validity results. Yet the vast majority of these studies are based on the DSM-IV [4] and not the new ASD criteria of DSM-5 [3].

To enhance ASD diagnosis accuracy, scholars recently adopted machine learning techniques, i.e. [8, 9, 25, 26]. The main goals of these studies were one or more of the following:

- Reducing the screening time
- Improving sensitivity and specificity
- Identifying the smallest number of ASD codes to simplify the problem

Machine learning methods offer automated efficient and effective classification models for the ASD problem since they adopt a mixture of mathematical and search methods from computer science [24]. Various different machine learning techniques have been recently applied by researchers to the ASD problem, e.g. decision trees [22], support vector machine [21], rule classifiers [1] and neural network [20]. ASD diagnosis is considered a typical classification problem in machine learning in which a model is constructed based on previously classified cases and controls. This model can then be employed to guess the new case diagnosis type (ASD, No-ASD).

This research paper pinpoints various issues related to ASD screening tools that require further investigation by scholars. The focus will be twofold:

1). Recent studies on machine learning in ASD to critically assess improvements in these studies especially the development of new machine learning methods for automatic ASD classification. We show recent results and challenges when machine learning is adopted for ASD classification which future studies can consider in order to improve the quality of the outcome. We believe that machine learning will be the next era in screening tools in which handcrafted classification methods will be replaced with automated predictive models. These models will guide clinical experts with fast yet accurate diagnosis decision.

2) Limited research has been conducted on identifying and evaluating ASD traits in the clinical environment especially under the DSM-5. Most of the current screening tools are not yet updated especially the diagnostic algorithms embedded within these tools. There is a need to revise most of the current ASD screening methods to reflect the new criteria of ASD according to the recently published DSM-5 manual.

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This paper is structured as follows: Section 2 is devoted to presenting the ASD diagnosis as a predictive classification problem. Section 3 presents two known clinical diagnostic methods along with research studies that review the need for updating screening methods to fulfil DSM-5. Moreover, the same section highlights and critically analyses related literature on the adaptation of machine learning in ASD research. Lastly, conclusions are given in Section 4.

2. ASD DIAGNOSIS AS A CLASSIFICATION PROBLEM

Figure 1 shows the ASD classification problem in machine learning. The input will be a training dataset of cases and controls that have already been diagnosed. Usually the cases and controls have been generated using a diagnostic instrument such as ADOS-R, ADI-R, etc. in a clinic and administered by a behaviourist, clinical psychologist or a licensed clinician specialised in that tool. Once the training dataset is identified then an optional step to reduce the data dimensionality by selecting a smaller set of features can be implemented. The aim of this step varies and is not limited to simplifying the problem, identifying the best ASD features, or reducing computing resources used during the data processing, etc.

Once initial data is processed then a machine learning algorithm can be applied. Currently, researchers usually employ ready software packages such as WEKA (Hall et al., 2009) to accomplish this task by loading the processed dataset and then choosing the machine learning algorithm. The outcome of this phase is that there are different measures that the end user can use to evaluate the effectiveness of the chosen machine learning method on guessing the type of diagnosis. Examples of the evaluation measures are accuracy, processing time, false positive rates, false negative rates, true negative rate, etc. Often these evaluation measures are embedded within the machine learning software package.

The process of ASD diagnosis described in Figure 1 elaborates the necessary steps taken to decide the type of diagnosis using machine learning. However, this process must be integrated in an existing common screening tool so it can be utilised by the appropriate domain expert. This scenario is still under research and has not yet been implemented. In other words, none of the existing screening tools actually contains a machine learning diagnosis algorithm that experts are using to arrive at the appropriate diagnosis type in ASD research. The classification process in machine learning should be automated rather than isolated and without appending the machine learning algorithm in an existing diagnostic tool the automation process is still 'unfinished business'.

3. LITERATURE REVIEW

Firstly, in this section, we briefly introduce two common clinical ASD screening methods. We then critically analyse recent research studies related to the use of machine learning in ASD research. Finally, we pinpoint the need for updating screening methods to meet the new DSM-5 ASD criteria.

3.1 ADOS AND ADI SCREENING TOOLS

3.1.1 Autism Diagnostic Observation Schedule

ADOS is one of the popular screening tools for Pervasive Development Disorder (PDD) and ASD that can be applied to children, adolescents and adults based on a structured set of activities with a certain module. Large numbers of clinical practices utilise ADOS for clinical diagnoses of ASD and PDD due to its reliability, validity, sensitivity and specificity. ADOS was designed by [14] as a semi-structured test that mainly evaluates an individual's behaviour related to language, social interaction and play (imaginary) to assess PDD and Autism traits and levels on any individuals under examination. There are four main modules developed in ADOS for children and adults in which each is applicable to a certain population based on the behavioural and language levels ranging from verbally fluent to non-verbally fluent. Usually the examiner selects the right module for each case under examination based on two factors: the chronological age and language proficiency [14].

Examiners during an ADOS session observe the individual behaviours related to the primary development areas of ASD via standardised activities. Social, language communication and other behavioural activities are evaluated when cases under consideration respond to the activities assigned to them and examiners record responses. The observation normally lasts around 30-45 minutes in which responses are recorded after the session by the examiner through coding them into a computerised tool. This tool contains a handcrafted diagnostic algorithm that computes a score for each case based on the responses, in order to

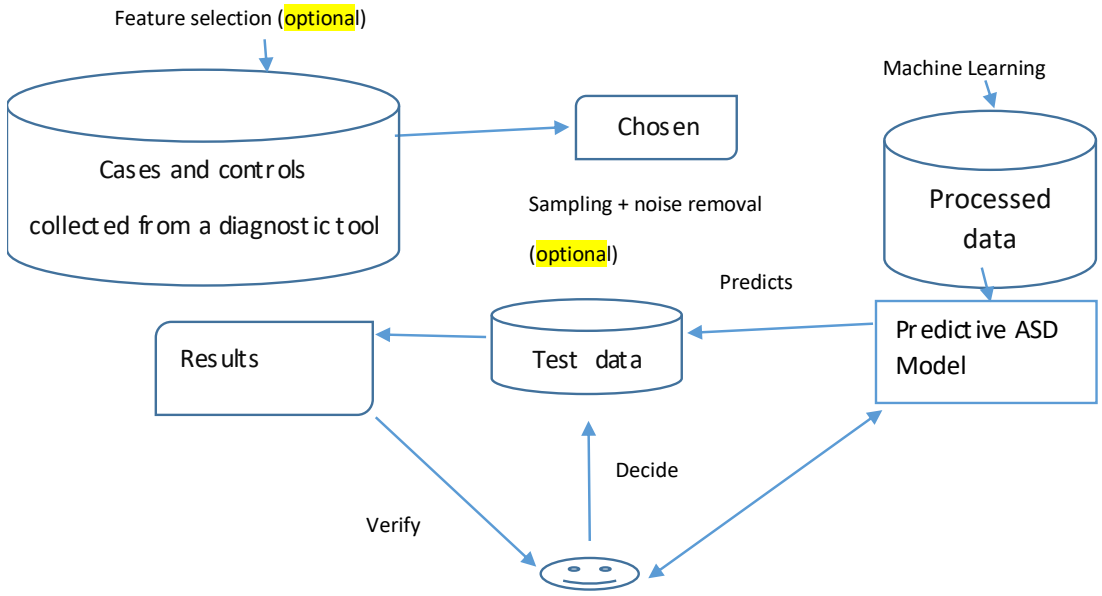

Figure 1: ASD diagnosis as a classification problem

come up with the right case diagnosis.

In ADOS, the four modules may overlap in activities but each module is designed to evaluate certain cases based on verbal speech and chronological age. For instance, module "1" is designed for cases that do not regularly utilise phrase speech (young children). Whereas module "2" is intended for children and linked with phrase speech that is not fluent and module; "3" is devoted for cases normally between 12-16 years' old who have fluent speech and who play with toys appropriate for their ages. Lastly, module "4" is intended to be applied on adolescent and adults who have fluent communication skills. Modules "3" and "4" have a high similarity although there is an exception which is related to the way social and communication data have been collected by the examiner, and whether it has been gathered during an interview (Module 4) or play (Module 3).

3.1.2 Autism Diagnostic Interview-Revised

ADI-R is a structured interview usually conducted by a clinician with the parent of individuals over 18 months old in a clinical session. ADI-R was developed in [15] to distinguish cases with PDD including autism from the non-spectrum disorder. The parent or caregiver will be given 93 different items / questions during the interview; primarily concerning previously observed behaviour of the child. The interview is split into five different phases (communication, restricted behaviour, play, and social development, general).

After the interview is terminated, the clinician utilises his knowledge and judgment to score each question from 0-3 as well as 7-9 where "0" indicates normality, and 1-3 correspond to a severity level from light to extreme. In addition, "7", "8" and "9" denote total abnormality, not applicable, or not known, respectively. Once all values are chosen for the 93 questions, a scoring algorithm computes scores for three major areas: "language and communication", "social interaction", "restricted and repetitive behaviour". The cut scores for the above behavioural areas are 8, 7, 10 and 3 respectively. A positive diagnosis is given when the computed scores for a case over all three areas meet or exceed the minimum cut-off scores [6]. Often ADI-R takes one to two hours to ~~be~~ conduct~~ed.~~ There have been some revisions on ADI-R aiming to shorten the time associated with the interview and enable it to be more appropriate for children under 3 years old.

3.2 CLINICAL TOOLS AND MACHINE LEARNING: A CRITICAL ANALYSIS

3.2.1 The Use of Machine Learning

[25, 26] claimed that machine learning methods such as decision trees can be employed to construct a model that contains fewer features than items found using ADOS-R (Module 1). Therefore, the time associated with the medical diagnosis is shortened without negatively influencing sensitivity, specificity, and validity of the test. The authors sought to identify the least number of items in ADOS-R to classify ASD cases via constructing decision tree classifiers in WEKA [10] by using information gain filtering. In particular, they have applied a number of machine learning methods (decision tree based) on an ASD dataset aiming to identify the best classifier.

The data set used in the experiment was downloaded from the Autism Genetic Resource Exchange (AGRE) repository [11]. The data set consists of 612 cases with autism and 11 cases of non-autism spectrum. The authors only kept two class labels (Autism and non-autism) and discarded all data examples that had over 50% missing values. After applying a number of decision trees based algorithms on the ASD classification data set, the results revealed that the best classifier in sensitivity, accuracy and specificity contains rules involving only eight features. They concluded that ADOS-R can only use eight features rather than the complete set of 29 features in Module 1. Nevertheless, the results are algorithm-specific since those eight features are only present in the Alternating Decision Tree algorithm (ADTree) and only for the specific data set used in the experiment. In other words, if for instance we apply other machine learning algorithms such as associative classification, rule induction or Neural Network, the number of features appearing in the classifiers may definitely vary.

A better approach toward achieving fewer numbers of features should result from investigating the complete features set significance on classification performance using feature selection methods. This may derive smaller features sets that are generic and not algorithm or data sensitive. One clear shortcoming of the data set(s) used in [25, 26] is the fact that it is clearly unbalanced and a third class/category of ASD is discarded which may simplify the problem of classification to either severe autism or no autism at all. This surely does not reflect the complexity of the problem, which contains overlapping data examples among class labels. In fact, some cases are hard to determine since they may belong to multiple categories which may confuse the algorithm. Eliminating these data examples may cause a generating of simple biased classifiers and therefore unreliable performance in terms of sensitivity, specificity and accuracy.

The process of clinical ASD diagnosis often takes between 30 to more than 120 minutes depending on:

1) The case complexity to be diagnosed
2) The clinical diagnosis procedure
3) The expertise of the clinical professional

Recent claims of speeding up the autism diagnoses procedure of ADOS-R (Module 1) based on machine learning techniques have been discussed earlier by [25, 26]. Nevertheless, obvious shortcomings related to the methodology used, data selection, evaluation measures and results analysis have been highlighted with rationales by [8]. The authors have argued that the problem of classifying autism using machine learning is not straightforward and requires careful consideration of the clinical procedure setup, algorithm design, and results interpretation as well as having sufficient data that represents all ASD categories. The following pitfalls in [25, 26] articles have been identified by [8]:

1) Despite the claim of the reduction of the number of features (codes) to eight in the ADTree classifier constructed from the input cases all tasks and activities of ADOS-R test must be performed and thus no administration time reduction is observed. Hence the full ADOS-R test must be conducted before building a classifier using ADTree algorithm in WEKA. Therefore, the claim is invalid.
2) The validation of ADOS codes can only be established within a clinical environment. Yet the authors of [25] have claimed that ADOS codes can be self-administered however this claim needs substantial supported evidence.
3) Data used are clearly imbalanced in terms of class labels. This should be reflected in the selection of the evaluation measures used rather than just picking up

"classification accuracy" which is usually biased when the class distribution in input data sets is imbalanced.

The process of clinical or non-clinical diagnosis of ASD can be lengthy since it may vary among cases and there may be other obstacles associated with the diagnosis process in the health care system. [2] have investigated the problem of shortening the time linked with ASD pre-diagnosis in family medical clinics. The aim was to enable medical care staff including physicians, nurses, and others utilising a ten-question form for a quick clinical referral of potential ASD cases. The authors have analysed different versions of current self-administered or parent assisted ASD screening tools, including:

- Quantitative Checklist for Autism Toddlers (Q-CHAT)
- Autism Spectrum Quotient (AQ) (3 versions)
    - Adult
    - Adolescent
    - Child

Samples of controls as well as ASD cases have been utilised to validate the different ASD traits in the three self-administered methods. The authors have used a web-based recruitment strategy as well as data already collected by their research group to measure the significance of each trait. The control data along with data from the cases have been split into training and validation sets respectively. The significant of a trait was computed using a discrimination index, which corresponds to the rate of positive cases for a trait, i.e. T, in the ASD training set from T rate, derived from the control training set. Different evaluation measures including specificity, sensitivity as well as "Area under Curve" (AUC) of the predictive validity have been adopted in the experiments. The top ten traits with discrimination scores have been selected, and the results of the ten selected traits showed competitive performance with respect to the abovementioned measures when compared with results obtained from the complete set of traits of each self-administered method. The authors concluded that these ten questions (traits) can only be used to refer suspected cases of ASD for full clinical screening and cannot be relied on for ASD diagnoses.

Few limitations are associated with this study; the imbalanced data set sizes when it comes to sub-categories of ASD diagnoses, and the participants' awareness of ASD among cases who participated in the online recruitment of data collection. These may create biased results. More importantly, we believe that despite the promising claim achieved by [2]; using only a discriminative factor is not sufficient to measure the significance of a code/feature in a self-administered method. There should be mathematical evaluations using information theory or wrapping methods on each feature within a large collection of sample of cases and controls. This will shift the problem to identify smaller sets of features as clusters. Each cluster contains features that possibly have relationships that guide the diagnostic algorithm when building classification models using predictive models. Therefore, we need to draw cut-off points that split features into groups that each contain correlated features. These groups of features may overlap in features where a feature / code such as x can possibly belong to multiple clusters. This is since data cases of ASDs within the original data set overlap in traits and the new ASD published criteria of the DSM-5 have similarities in sub-category items (codes) (The A's-items, B's-items, etc.).

ASD is often diagnosed by an expert paediatrician or child behaviourist within a clinical review of the patient's behaviour, language, senses, etc. Usually, this approach of ASD diagnosis is called "Clinical Judgment" and it is the widely used method for ASD classification among children. [28] proposed a method for classifying children's ASD levels through a combination of patients' parents' interviews and clinical observations. The main intention for that research was to determine the causes of the ASD and to differentiate among different groups of ASD especially with regard to children. The conducted parents' interviews including a clinical observation claimed to:

a) Clearly categorises children into different groups so common characteristics within the same group and differences with other groups can be identified, and,

b) Resolves major differences between clinical observation and reports obtained from the children's parents' interviews.

The authors have used data from "Study to Explore Early Development" (SEED) (http://www.cdc.gov/ncbddd/autism/seed.html) that involved over 2600 children who were categorised as "having ASD" and "not having ASD". The proposed ASD classification method seems promising and it was able to classify most of the children cases into well-defined groups based on their ASD level. This can assist the process of treatment as well as near future research.

3.2.2 Clinical Tools and DSM-5

After the DSM-5 was published, several studies, i.e. [12, 13, 19] pointed out that some clinical cases who used to be classified under "Autism" or its related disorders using DSM-IV criteria may not qualify for the new class (ASD) if DMS-5 criteria are used. This has created a debate since results related to different experimental studies from 2012 onward showed inconsistencies in the sensitivity and specificity evaluation measures. For example, [17] revealed a significant decrement in sensitivity for both low functioning adults and at-risk toddlers. [19] results showed that cases related to Asperger's disorder may be misclassified or missed by the screening methods used if the criteria of diagnoses are based around the DSM-5.

[16] have reviewed eleven adult screening tools for ASD including AQ, Adult Asperger Assessment (AAA), ADI-R, Asperger Syndrome (and high-functioning autism), Diagnostic Interview (ASDI), ADOS – Generic (ADOS-G), and six others. The review has focused on the sensitivity and specificity measures as well as the validity for the test for the adult population. For each screening tool, a description of the tool, number of categories used, number of items involved, any possible versions of the tool and briefing results if exist, have been highlighted. Most of the tools reviewed are not self-assisted and are based on questionnaire(s), interviews, and observation and are held within a medical clinic under clinician's supervision. The authors have concluded that there is a need to develop standardised ASD screening tools for adults in order to track autistic traits in adulthood and therefore assist the diagnostic and design proper treatments plans.

[13] studied the impact of DSM-5 criteria on sensitivity and specificity measures to validate whether the new criteria have pitfalls in misclassifying cases that have been qualified according to the DSM-IV criteria and not by DSM-5 ASD criteria. DSM-5 criteria have been mapped to items in a known screening method called Diagnostic Interview and Communication Disorder (DISCO); three DISCO versions are implemented that actually embed the new items of the DSM-5 into two major sub-domains. Primarily, they implemented the following DISCO versions:

- The first included the minimum requirement proposed in the DSM-5, i.e. only one behavioural item was necessary for each sub-domain.
- The second version implemented the Youden J Statistic to determine the optimal thresholds for both sensitivity and specificity: J = Sensitivity + Specificity − 1.
- The third version involved picking up the largest numbers of behaviours that maintained the maximum sensitivity in the sub-domain.

The aim was to balance the specificity and sensitivity of the above versions on two datasets that were used earlier. The size of the two datasets was 82 and 115 respectively, and both are related to clinical diagnoses using DISCO-9 [27]. Two validation phases to map DISCO 300 items to the new DSM-5 sub domains' items have been conducted using experts in autism, clinical psychology, and DISCO screening methods. After conducting the experiments against the two samples' data, the results showed that the third version modified DISCO methods to produce a balance between specificity and sensitivity thresholds. Moreover, the initial DISCO method (version 1) produced the highest sensitivity but the lowest specificity whereas Youdens' version had the lowest sensitivity and highest specificity. Overall, the new criteria proposed in the DSM-5 did not largely influence the diagnosing process of ASD and produced similar results to DSM-IV methods, at least on the datasets considered in this study. The smaller number of cases in the data samples can be considered one of the limitations of this study. Additionally, no "actual" clinical diagnoses have been conducted in order to verify the results reported. Nevertheless, this study has showed the need to validate most existing diagnostic tools of ASD by considering versions that are mapped to the new ASD criteria of the DSM-5.

A meta-analysis research study, from [5], investigated the expected ratio of a selected population with an autism classification under the DSM-IV compared with the new DSM-5. The study has used previously published results from over twenty autism studies to seek eligibility of already diagnosed autism cases based on the DSM-IV compared with the new criteria of DSM-5. The results showed that cases with PDD-NOS are the least likely to be classified with ASD under the DSM-5 manual with fewer than 50% cases followed by cases diagnosed with Asperger Syndrome.

4. CONCLUSIONS

The classification process within machine learning is automated and 'on the fly', not a standalone problem with a static training data. Rather, it is a complex dynamic process integrated with a screening tool in the presence of appropriate medical staff inside a clinical environment. Unfortunately, recent studies on the use of machine learning in ASD research focusing on the diagnosis separates the machine learning from the diagnostic tool and deals with the ASD problem statically, whereas existing machine learning algorithms are merely applied on an historical dataset of cases and controls. In this paper, we focused on recent machine learning studies that tackled ASD as a classification problem and critically analysed their advantages and disadvantages. Moreover, we showed the necessary steps required to claim the development of intelligent diagnostic tools based on machine learning by replacing the handcrafted rules inside the ASD screening tools with a predictive model. Lastly, we highlighted the urgency of updating ASD clinical screening tools to reflect changes proposed in the DSM-5 manual. The dissemination of the DSM-5 demanded a change in the way that the diagnostic algorithm coded within the ASD screening tool behaves in the process of classifying cases. There is a need to re-examine questions or features within the ASD diagnostic tools to fulfil the new criteria of the DSM-5. This requires mapping the new ASD criteria to the features or attributes used in the clinical diagnosis tool as well as evaluating the way the diagnostic algorithm works. The adjustment will direct researchers to how the different Pervasive Development Disorders (PDD) overlap in the new DSM-5 criteria and this will help with improving current diagnostic tools.

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