A Machine Learning Approach for the Automated Diagnosis of ADHD: Implications and Significance for Sustainable Youth Development Policies

Shubh Khanna, International Development Researcher, Hunter College HS (corresponding author)
shubhkhanna@hunterschools.org
(646) 617-3631
220 Riverside Boulevard, Apartment 18A
New York, NY, 10069
William Das, Deep Learning Researcher, Hunter College HS

I. INTRODUCTION

Equitable access to medical diagnosis is integral to achieve sustainable development goals in the developing world, where poverty and a lack of medical institutions create stark inequalities in the accessibility of medical diagnosis and treatment. Attention-deficit/hyperactivity disorder (ADHD) is the most pervasive neurodevelopmental disorder in the world, particularly in sub-Saharan Africa and Latin America: the prevalence rate, according to a 2007 sample study, is 8.5% and 11.8%, respectively, compared to a 9.2% prevalence rate in the U.S..1

Yet, despite the similar prevalence rates in the U.S. and developing nations, ADHD and similar neurobehavioral disorders remain widely underdiagnosed in the developing world as a result of both societal stigmas on youth neurological disorders2 and deficient medical practices.3 The underdiagnosis and neglect of ADHD in countries across the globe is particularly exacerbated in developing nations that lack functional healthcare systems and accessible diagnostic services; this renders governmental efforts for increased educational opportunities ineffective because the child is not able to receive the proper treatment and academic support for ADHD. Chinawa et al. note the egregious neglect of ADHD in developing countries, notably Nigeria, where the reported prevalence rate is uncharacteristically low despite the high prevalence rate in neighboring developing nations.4 Lower prevalence rates in rural areas of certain countries can be attributed to the inaccessibility of diagnostic services, which precludes the administration of proper treatment regimens, thereby pushing the next generations of the rural poor into greater socioeconomic struggles.5 Ginsberg et al. strongly emphasize that despite being severely debilitating for those who are left untreated, ADHD is overall egregiously

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4 Ibid.
underdiagnosed and undertreated. Untreated ADHD, synergized with the likely presence of comorbid disorders, leads to severe academic, socio-emotional, occupational, and behavioral impairment.

The long-term effects of untreated ADHD, stemming from inaccessible diagnosis, are detrimental for individuals and their families. Children and adults with untreated ADHD suffer from poor educational outcomes, familial relationships are negatively impacted due to increased economic burdens and heightened conflicts, and affected individuals are more likely to engage in reckless criminal behavior and often engage in substance use, nicotine addiction, and alcohol abuse. Untreated ADHD during childhood is a risk factor for later adult mental health issues. Lack of treatment impacts social and occupational functioning and increases the likelihood of developing comorbid disorders such as heightened anxiety, depression, personality disorders, and antisocial behaviors. Furthermore, inaccurate clinical evaluations can lead to inappropriate treatment interventions, such as wrongly administering stimulant drug medications that can have side effects on healthy children.

Moreover, in developing nations, the underdiagnosis of ADHD diagnosis pushes poorer families further into poverty traps that mitigate many of the benefits of education, and consequently cause future generations to have poorer economic opportunities. The risks that stem from inaccessible diagnosis of ADHD exacerbate economic inequality and push poor households that cannot afford diagnosis into multigenerational poverty. Not being diagnosed with ADHD creates an inability for the youth to succeed academically and socially, which limits their economic opportunities as they grow of age in the workforce. This missed economic potential, however, can be mitigated through the implementation of efficient and early diagnosis of ADHD and similar neurobehavioral disorders, which have been perennially neglected in developing nations. A critical factor in development is the economic inequality that results from a lack of access to healthcare — this prevents individuals from succeeding in the workforce by hindering the administration of proper treatment regimens. Early and efficient diagnosis of ADHD, and similar neglected neurobehavioral disorders in the developing world is therefore critical to effectively administer treatments and prevent subsequent complications for a child’s socioemotional development, academic and occupational achievement, and overall welfare. Efficient diagnosis of this disorder, thus, is crucial to effectively administer treatments and prevent subsequent

8 Ibid.
complications for a child’s socioemotional development, academic and occupational achievement, and overall welfare.

A. Current Diagnosis
Current clinical diagnosis fails in developing nations for two reasons: it is inaccessible and inaccurate. There is no objective test to diagnose ADHD. Diagnosis is based solely on observed behavior and reported symptoms, creating a risk of over and under-diagnosis. Clinical tests cost between $800-$2000 per screening, making diagnosis for ADHD inaccessible to a majority of the world and general population. Evaluations are based on a checklist of eighteen symptoms, nine related to inattention and nine related to hyperactivity and impulsivity. These subjective clinical assessments – the only way doctors are able to evaluate ADHD – often last multiple hours. Moreover, the demand for these examinations greatly exceeds the maximum capacity of available developmental pediatric clinics. As a result, children are often waitlisted for over a year, preventing timely diagnosis and delaying the start of necessary treatment. Wait times can extend beyond 13 months for minorities or socioeconomically disadvantaged groups. Medical experts collectively agree that the lack of an objective mechanism to characterize ADHD remains an unsolved and pervasive problem, precluding effective and accessible treatment regimens.

Moreover, the timely and expensive diagnosis of ADHD exacerbates socioeconomic divides across the globe: racial and ethnic minorities have been reported to be diagnosed with ADHD at lower rates than white children, and therefore have unmet treatment needs. Black children are diagnosed at only two-thirds the rate of white children despite displaying greater symptomatology. Moreover, Hispanic children are also severely under-diagnosed. Thus, treatment for ADHD remains primarily based on socioeconomic means of certain families, as evident by the diagnostic prevalence rates between socioeconomic groups. As such, a universal, freely accessible method to diagnose ADHD is necessary in order to bridge these socioeconomic gaps and break the barriers that preclude minority groups from being afforded proper treatment around the globe, particularly in developing countries.

B. Pupillometric Variation in ADHD
Due to the currently deficient methods for diagnosing ADHD, an objective and reliable mechanism to characterize the disorder is necessary in order to ensure accurate, timely, and cost-effective diagnoses in developing nations. Oculomotor paradigms are particularly adept in

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17 Duda et al., “Use of machine learning for behavioral distinction of autism and adhd,” 733.
19 Duda et al., “Use of machine learning for behavioral distinction of autism and adhd,” 733.
20 Ibid.
21 Ibid.
22 Hamed et al., “Why the diagnosis of attention deficit hyperactivity disorder matters,” 169.
tracking maturational abnormalities in brains affected by neurodevelopmental disorders. A promising biomarker specifically for ADHD in humans is pupil-size dynamics — the ways in which the pupil responds to certain visual stimuli. Pupil-size dynamics have been shown to reflect the state of the brain norepinephrine (NE) system, which controls executive functioning and is impaired by ADHD. Geng et al. showed that pupil size reflects uncertainty in users who completed a visuospatial working memory task. Wahn et al. showed that pupil-size dynamics can be utilized as a reliable metric to assess attentional load in patients. Given the vast literature highlighting correlations between pupillary responses and attentional performance, it was hypothesized that pupillometric features could be utilized as an objective biomarker to effectively characterize ADHD. We sought to develop a machine-learning based method to create an automated and free diagnostic application for the developing world that could analyze pupillometric variation in subjects, hypothesizing that it would accurately reflect behavioral differences between ADHD positive and control subjects.

C. Applications of Machine Learning

Babiker et al. developed a machine learning model to predict a user’s emotional state using pupillometrics, with an accuracy of 96.5%, sensitivity of 97.93%, and specificity of 98%, engineering a set of features based on pupil dilation velocity and acceleration. Qian et al. devised a machine learning-based decision fusion model to classify visual responses based on similar pupillometrics. Baltaci et al. also incorporated a machine learning-based model to evaluate pupillometric variation in human subjects in order to classify user’s stress response and mental state, extracting a variety of statistical features from the pupillometric data.

As such, we sought to develop a machine learning-based method to analyze pupillometric variation in subjects, hypothesizing that it would accurately reflect behavioral differences between ADHD positive patients and control subjects. This model could then be implemented in a freely accessible web based application that uses a standard camera to capture biometrics in real-time and analyzes pupillometric data with an optimal machine learning algorithm. By extracting a comprehensive set of features from pupil-size data, we hypothesized that an accurate and accessible mechanism to diagnose ADHD could be developed using a machine learning-based methodology. Moreover, using these engineered features, we sought to extract valuable biometric patterns from the pupil size data to advance current understandings of pupillometry regarding the presence of ADHD. The culminating product of this study was a freely accessible web application that can serve as a novel mechanism to diagnose ADHD in developing nations plagued by egregious underdiagnosis rates.

24 Wainstein et al., “Pupil size tracks attentional performance in attention- deficit/hyperactivity disorder,” 8225.
25 Ibid.
II. DATASET
A group of 50 subjects participated in an IRB-approved study, yielding a declassified dataset of 67 instances.\(^\text{31}\) 28 subjects were patients diagnosed with ADHD (4 girls, 24 boys), and 22 were healthy control patients (3 girls, 19 boys), recruited from local schools and ages ranging from 10-12 years. A subgroup of 17 ADHD patients performed the task twice, on and off medication.

All subjects were required to complete a visuospatial working memory task which consisted of multiple 8 second trials, during which their pupil-sizes were measured. In the first five seconds, three dot arrays were presented, followed by a distractor image. In the last three seconds, subjects were presented with a random dot array and asked to determine if the dot had been presented to them previously in the first three images.

III. METHODS

A. Pupil Size Visualization and Analysis
Line plots, box plots, violin plots, as well as point plots were constructed in order to garner intuition on pupillometric variation between ADHD positive and negative subjects. For each patient, the mean pupil size across all trials throughout the time-series was calculated and grouped by ADHD diagnosis. Statistics were gathered from this data and utilized to engineer robust features.

B. Feature Extraction
As shown in Table 1, a number of pupillometric features were extracted from each trial in order to feed into the machine learning models. Since each patient completed 160 trials, the features listed in Table 1 were calculated for each trial and averaged for each patient. Let \( P_0 \) denote the timestamp marking the presentation of a probe, and \( P_i \) denote the time interval from 5000ms-7000ms.

Given a starting timestamp \( T_0 \) and pupil size \( P_0 \), the pupil size dilation velocity \( V_i \) at any given timestamp \( T_i \) with pupil size \( P_i \) is given by:

\[
V_i = \frac{P_i - P_0}{T_i - T_0}
\]

The acceleration \( A_i \) is given by:

\[
A_i = \frac{V_i - V_0}{T_i - T_0}
\]

The accumulated pupil dilation velocity \( AV_i \) is the sum of: \( V_0 + V_1 + \ldots + V_i \).

\(^{31}\) Wainstein et al., “Pupil size tracks attentional performance in attention-deficit/hyperactivity disorder,” 8227.

\(^{32}\) Ibid.
C. Machine Learning Algorithms

The following state-of-the-art binary classification algorithms were trained using the engineered features: Logistic Regression, KNN Neighbors, Random Forest Regression, Gradient Boosting Classifier, Naive Bayes, Decision Tree Classifier, and AdaBoost Classifier. A comprehensive evaluation of each algorithm was conducted, taking into account accuracy, precision, recall, $F^1$ scores, as well as 5-fold cross-validation (CV) metrics and the area under the receiver operating characteristic (AUROC). Recursive feature elimination (RFE) and forward feature selection were employed in order to increase model performance. Both methods are iterative and reduce the number of parameters inputted into a model in order to choose those that are strongest in classifying between the two groups.

D. Accessible Diagnostic Application

![Image]

**Fig. 1:** Web application capturing and segmenting the pupil in real-time.

In order to incorporate the optimal machine learning model, a web application was engineered as a novel diagnostic mechanism for ADHD. The optimal machine learning model was serialized into the backend of a web application that records pupil biometrics in real-time, returning an output of a probability of diagnosis, as well as medical advice. The web application simulates the visuospatial working memory task used in Wainstien et al.’s study.
The web application uses convolutional neural networks (CNNs) to detect the head and circle hough transform methods to segment the iris, followed by a custom ray tracing algorithm to measure the diameter of the pupil. It utilizes the built-in GPU on a mobile phone or computer, accessing JavaScript/WebGL based libraries to perform segmentation and diagnosis in real-time.

IV. RESULTS

A. Feature Visualization

1) Line Plots:
Figures 3 and 2-5 illustrate time-series line plots for the mean pupil diameter, as well as pupil dilation velocity and acceleration, grouped by diagnosis of ADHD. Figure 3 illustrates the mean pupil size averaged across all trials for ADHD positive and negative groups. ADHD negative control subjects exhibit increased variation in eye movements and greater mobility throughout the 8s interval. Moreover, the maximum pupil size after the presentation of a probe is noticeably larger for control subjects. The minimum pupil size from the 7s mark is also noticeably smaller for control subjects. Moreover, ADHD positive subjects exhibit predominantly lessened dilation acceleration and velocity following the presentation of a stimulus.

2) Box and Violin Plots:
Figures 6-9 illustrate box and violin plots for two statistically significant features (p < .05).
B. Pupil Dynamics Statistics
Tables II-IV exhibit statistically significant standardized values (p<0.05), calculated for ADHD positive and negative groups. During the presentation of a visual stimulus, the standard deviation and variation in pupil-size for ADHD positive subjects were significantly lower than that of control subjects. Moreover, the local maxima was considerably lower, as well as the median and interquartile range.

<table>
<thead>
<tr>
<th>Group</th>
<th>$\sigma$</th>
<th>$\sigma^2$</th>
<th>Local Maxima</th>
<th>Median</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>0.4343</td>
<td>0.1886</td>
<td>1.0514</td>
<td>0.7658</td>
<td>0.5706</td>
</tr>
<tr>
<td>Negative</td>
<td>0.5206</td>
<td>0.2711</td>
<td>1.3858</td>
<td>0.9370</td>
<td>0.7959</td>
</tr>
</tbody>
</table>

C. Classifier Results
1) Binary Classification Metrics:
State-of-the-art machine learning algorithms were evaluated based on several key classification metrics: accuracy, precision, recall, average precision-recall rate, F-1 Score, 5-fold CV score, as well as AUROC. The Naive Bayes model achieved the optimal classification metrics, with 0.9412 accuracy, 1 precision, 0.9091 recall, 0.9679 average precision-recall rate, 0.9524 F-1 Score, 0.9545 AUROC, and 0.8867 5-fold CV score. The sensitivity, which measures the percentage of positive subjects correctly identified as such, was .9091.

2) Confusion Matrix:
The model correctly predicted 10 out of 11 subjects diagnosed with ADHD as having ADHD, and correctly predicted 6 out of 6 healthy subjects as not having ADHD.

3) AUROC:
Figure 10 illustrates the AUROC curve for the Naive Bayes model when applied to the test data, with a value of 0.9545.

<table>
<thead>
<tr>
<th>Group</th>
<th>$\sigma$</th>
<th>$\sigma^2$</th>
<th>Local Minima</th>
<th>Median</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>0.5146</td>
<td>0.2648</td>
<td>-0.4289</td>
<td>0.3734</td>
<td>1.0299</td>
</tr>
<tr>
<td>Negative</td>
<td>0.7233</td>
<td>0.5232</td>
<td>-0.5683</td>
<td>0.4056</td>
<td>1.5567</td>
</tr>
</tbody>
</table>

Fig. 10: AUROC curve of the Naive Bayes Classifier.
IV. DISCUSSION

A. Machine Learning Robustness

This study utilized a dataset of 67 instances — as such, 5-fold CV, a benchmark validation method, was applied to best assess the generalization ability of classifiers and ensure that sufficient training data was inputted into the models. To account for the sparsity in data, data augmentation techniques were also utilized, ensuring that as much training data was available to boost model performance. This ensured that a robust and applicable machine learning model could be utilized in the backend of an accessible web application.

<table>
<thead>
<tr>
<th>TABLE V: Binary Classifier Metrics</th>
<th>TABLE VI: Additional Binary Classifier Metrics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>Model</td>
</tr>
<tr>
<td>Logistic Regression</td>
<td>Logistic Regression</td>
</tr>
<tr>
<td>Random Forest</td>
<td>Random Forest</td>
</tr>
<tr>
<td>Decision Tree</td>
<td>Decision Tree</td>
</tr>
<tr>
<td>Naive Bayes</td>
<td>Naive Bayes</td>
</tr>
<tr>
<td>KNN Neighbors</td>
<td>KNN Neighbors</td>
</tr>
<tr>
<td>AdaBoost Classifier</td>
<td></td>
</tr>
<tr>
<td>Accuracy</td>
<td>Precision</td>
</tr>
<tr>
<td>Logistic Regression</td>
<td>0.7059</td>
</tr>
<tr>
<td>Random Forest</td>
<td>0.7059</td>
</tr>
<tr>
<td>Decision Tree</td>
<td>0.6471</td>
</tr>
<tr>
<td>Naive Bayes</td>
<td>0.9412</td>
</tr>
<tr>
<td>KNN Neighbors</td>
<td>0.7647</td>
</tr>
<tr>
<td>Support Vector Machine</td>
<td>0.7059</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TABLE VII: Confusion Matrix of Naive Bayes Classifier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actual (NO)</td>
</tr>
<tr>
<td>Actual (YES)</td>
</tr>
</tbody>
</table>
The excellent AUROC and recall values indicate the strong binary classification ability of the ensemble model — 90% of affected individuals are correctly classified with ADHD, while the accuracy of the binary classifier at varying thresholds reaches 90%, indicating its overall strength in differentiating between ADHD positive and negative subjects. These metrics significantly outperform the current misdiagnosis rate reported to be around 20%,33 paving the path for a novel diagnostic method for one of the world's most commonly misdiagnosed and stigmatized disorders, specifically in developing nations.

B. Applications and Potential to SDG 3.8

The web application developed offers a novel and reliable technical approach to diagnose ADHD that is time-efficient, freely accessible, and reliant on an objective biomarker, rather than inaccurate subjective evaluations. This novel approach to diagnosing a widespread neurobehavioral disorder has the ability to allow children across the world to receive the help and support they need to reach their academic and occupational potential. Moreover, the eye tracking methodology innovated in this research can be implemented across different neurodevelopmental conditions, thereby democratizing access to screenings for other disorders that are often neglected in developing nations.

The implications of this work in developing nations are significant. The expected prevalence of ADHD is nearly equivalent in sub-Saharan Africa and Southeast Asia, but the number diagnosed is far less than in the United States and other highly developed nations. In developing nations, the inaccessibility of diagnosis, coupled with traditional stigma surrounding mental disorders, precludes proper diagnoses and treatments for youth. The Sustainable Development Goal 3.8 of the United Nations’ 2030 Agenda for Sustainable Development affirms the importance of equitable medical diagnosis and support: "access to quality essential health-care services" in addition to "effective, quality, and affordable essential medicines" are vital to create a platform for developing nations to thrive in the medical sector and reach those who need it the most.

This research has the potential to catalyze equitable access to the medical diagnosis of ADHD, supplementing SDG 3.8 to improve the lives of those who have certain disorders and are neglected in developing nations. The application has proved through clinical trials to be effective and easily used without the support of a medical practitioner, opening its applicability to rural areas with few medical doctors. Through its accessibility and accuracy, the developed application’s potential impacts in the developing world lie in breaking socioeconomic barriers surrounding ADHD and other neurobehavioral disorders that pervade the youth in nations across the world. Rather than going through lengthy clinical diagnosis procedures, patients can use this web-based application to test for the presence of ADHD, without the assistance of a clinician. This application has the ability to reach those who have unmet treatment needs for one of the most neglected disorders in the developing world by providing an accurate and efficient diagnosis. Transcending the boundaries of simple diagnostics, our software provides medical advice and future measures to take based on the probability of having ADHD. Its impacts are not strictly limited to the developing world, as this application provides a new foundation for institutions across the world to diagnose ADHD, reliant on the objective biomarker of pupil-size dynamics, rather than loose qualitative observations.

At the same time, this work also emphasizes the changing landscape and role of both the public and private sector on working towards making medical diagnosis accessible for a majority of the developing population. In a nation that lacks many medical institutions and experienced medical practitioners, automated diagnosis is likely the most relevant application of artificial intelligence to support populations and sustain growth.

VI. CONCLUSION
Through the development of a machine learning-based method to analyze pupillometrics from ADHD positive and negative subjects, this study culminated in the creation of a novel diagnostic test for ADHD. Using the developed model, a web application that captures pupil biometrics in real time during an administered memory task was developed. This diagnostic application feeds data into the optimal machine learning algorithm and outputs a probability of diagnosis, as well as medical advice. This novel method offers a time-efficient, accurate, and accessible technical approach to diagnose ADHD. Moreover, through its accessibility and accuracy, the application's potential impacts in the developing world lie in breaking socioeconomic barriers surrounding ADHD and other neurobehavioral/neurodevelopmental disorders that pervade the youth in nations across the world. Our research paves a new path for engineering public policy geared towards the youth by also emphasizing the importance of furthering research and policies to improve stigma and medical practices regarding neurobehavioral disorders. If governments across the world focus on addressing these mental disorders that impair an individual's ability to succeed in the workforce, members of the younger generation can be included in the economy in an unprecedented way. Our research serves as the stepping stone for implementing these policies.

VII. REFERENCES


27. R. L. van den Brink, P. R. Murphy, and S. Nieuwenhuis, “Pupil diameter tracks lapses of attention,” PloS one, vol. 11, no. 10, pp. e0 165 274–e0 165 274, 2016.