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Assessment of Heart Rate Variability Response in Children with Autism Spectrum Disorder using Machine Learning

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Abstract: Autism spectrum disorder (ASD) is a developmental disability that involves persistent challenges in social interaction, communication and behaviour. The purpose of this study is to apply a machine learning approach to differentiate between autistic and normal children and to evaluate the performance of different classifiers in the detection of autism disorder. Heart Rate Variability (HRV) analysis is one of the strategies used for ASD detection by assessing the autonomic nervous system (ANS), which serves as a biomarker for the autism phenotype. HRV can be derived from the photoplethysmogram (PPG). Logistic Regression, Linear Discriminant Analysis and a Cubic Support Vector Machine (SVM) were chosen to evaluate the performance of HRV features in differentiating between normal and autistic children. Three different combinations of features were selected out of 19 features in total. From the results, Logistic Regression was the best classifier to differentiate between autistic and normal children in a colour stimulus test with 100% accuracy, while Linear Discriminant Analysis was best suited in the baseline test with 90% accuracy. In conclusion, the machine learning approach could be an alternative method of making an early diagnosis of ASD in the near future.

Keywords: Autism spectrum disorder, heart rate variability, machine learning

1. Introduction

Autism spectrum disorder (ASD) is a developmental disability that involves persistent challenges in social interaction, communication and behaviour. Autism is known as a "spectrum" disorder because the types and severity of symptoms are broad and vary from person to person. Autism is more likely to occur in males than females with a 4:1 ratio, with a prevalence of 6 per 1000 children. Due to the rising rate of ASD, increased awareness of the condition and more services for children with ASD are important. A decrease in the age of diagnosis is a highly important contributor to the elevated prevalence of ASD [1]. Symptoms of ASD often show in early childhood and interfere with daily function [1]. The root cause of autism spectrum disorder has not been discovered. There are probably many causes, such as genetics and environmental factors, leading to ASD with different complexity levels, symptoms and severity [2]. Children and adults with ASD may face difficulties, including an inability to live independently, social isolation, employment problems, victimisation and being bullied. Therefore, early diagnosis and intervention are extremely helpful in managing the symptoms of ASD and improve behaviour, skills and language development.

Early detection and treatment are the most important steps that can be taken to decrease the symptoms of autism spectrum disorder and improve the quality of life of ASD sufferers. However, diagnosing ASD can be difficult because there is no medical test, such as a blood test, to diagnose the disorder. ASD symptoms are usually recognised by

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observation and the use of checklist instruments, which leads to subjective and uncertain interpretation. Raj reported that detecting and starting treatment of ASD at the age of 18 to 24 months can increase a child's IQ by up to 17 points [3]. However, ASD is rarely diagnosed before a child is 24 months old as the symptoms may not show until that age or later. This delay means that children with ASD might not get the early help they need. Therefore, it is essential to develop a method that can diagnose autism before patients are 24 months old so that early treatment can be given for their growth development.

Machine learning is an application of artificial intelligence (AI) that enables systems to access data, and it can automatically learn and improve through experience without being explicitly programmed. Previous studies have shown that machine learning can differentiate between normal and ASD children [4-7]. Hence, a machine learning approach based on these findings was devised to overcome the limitations of the current methods of diagnosing ASD. Moreover, having such a method for the early diagnosis of ASD that is precise, not time-consuming, based on physiological HRV data and not subject to a practitioner's observation offers an opportunity to monitor and assess children with ASD over their time of growth to evaluate their ASD stage. However, previous studies have used MRI [6,7] and eye trajectory measurement [5] which require a more complicated set-up and are more time consuming.

Cardiovascular autonomic disease is possibly associated with the pathogenesis of ASD in children [8]. This has increased the interest in developing diagnostic strategies for ASD by assessing the Autonomic Nervous System (ANS) to study the autonomic function of children suspected to have ASD. ANS regulates bodily functions through the parasympathetic and sympathetic branches. The parasympathetic branch modulates the rest-and-digest response, while the sympathetic branch initiates the fight-or-flight response. Children with autism and who demonstrate hypo- or hyper-reactivity to sensory stimuli would, therefore, display atypical ANS activity. Therefore, autonomic dysregulation may serve as a biomarker for the ASD phenotype and can be used to distinguish the sensory reactivity in ASD children from that found in normal children [9]. This ANS activity can be assessed by using Heart Rate Variability (HRV) [10,11].

HRV, the fluctuation in the time intervals between adjacent heartbeats, is an evolving property of interdependent regulatory systems that work to help practitioners respond to environmental and psychological challenges on various time scales. HRV analysis have become a promising empirical measurement of controlled emotional activity which on one hand is also the core attribute of ASD symptom. Analyses from many studies have found that HRV and ASD behavior is strongly correlated [4, 12-14]. Hyperarousal which is higher sympathetic and lower parasympathetic behaviour has been found correlated with ASD during rest state [15]. Other research reported lower high frequency (HF) which indicate lower parasympathetic activity in children with ASD who have been schooled during rest periods [16]. Lower parasympathetic behavior means that these children are more stressful and unable to control self-reliance and stay activated. On a qualitative scale, a study has recorded that the fewer level of PNS behavior during attention to a picture for children aged 12, with or without ASD, has been related to impaired socialization abilities [17]. For adolescents aged 7-17 years, lower HRV was also observed in the ASD community while sitting quietly, and not in the control group, which demonstrated slower general emotional awareness in contrast with the ASD group [18]. The measurement of HRV can be performed using photoplethysmography (PPG), which is more convenient compared to an electrocardiogram (ECG) [2].

PPG is a simple optical technique used to detect volumetric changes in blood in the peripheral circulation. It is a low-cost and non-invasive method that makes measurements at the surface of the skin. PPG-based medical devices are widely used in various clinical set-up applications, such as clinical physiological monitoring, blood pressure and variability in heart rate. In addition, the PPG signal is used to examine the autonomic control of the cardiovascular system. It has been shown that PPG signal peaks coincide with the R peaks of the ECG in normal subjects [19]. This result has led to current investigations of whether, in the case of abnormal subjects, the PPG signal reflects cardiac activity and R-R interval variability [20]. In addition, recent work has proven that PPG-derived HRV can be fed into machine learning and has performed successfully in classifying ASD and normal children [2]. However, this study only compared the Support Vector Machine and the Shallow Neural Network. Therefore, this study investigated different types of machine learning for the assessment of the HRV response in ASD children and Typical Development (TD) children.

2. Method

A total of ten subjects, consisting of five subjects clinically diagnosed with ASD and five TD subjects, all of whom were children between the ages of 8 to 12, participated in this study. All subjects had undergone two different tests to acquire their PPG signal. The HRV signal was then derived from the PPG signal before a feature extraction process was undertaken, which resulted in 19 different features. The PPG signal acquired during a rest state was labelled as the baseline test. As it is difficult for young children to sit calmly, a special measure, the "Calm Viewing" protocol, was carried out [21]. Based on the "Calm Viewing" protocol, the children were required to watch a four-minute nature video to ensure they sat calmly with no interruption during the recording process, while the PPG signals were acquired for the baseline test. Another test was a colour stimulus test, where the subjects were visually stimulated with different colours while their PPG signals were acquired. The colour stimulus theory uses the retina of a human, which contains rod and cone cells. The cone cells distinguish the colour while the rod cells detect the amount of light. There are three types of cone cell, which vary according to the peaks of their spectral sensitivities, identified as Short (S), Medium (M) and Long (L). Every colour has a different wavelength, which gives sensitivity to the cone cells to detect blue (short-wavelength),

green (medium-wavelength) and red (long-wavelength) light, respectively. The brain connects each cone cell's information to produce different perceptions of various colours; therefore, the strength elicited from varying stimuli means different colours will vary.

Next, three different combinations of HRV features were fed into the three classifiers to choose the optimum combination for distinguishing between ASD and TD children. The three combinations include the following 19 features:

- RMSSD - Root mean square successive difference.
- SDANN - Standard deviation of the average of normal-to-normal intervals.
- SDNN - Standard deviation of R-to-R interval.
- HTI - HRV triangular index.
- HF - High frequency.
- LF - Low frequency.
- VLF - Very low frequency.
- TP - Total power.
- LFnu = LF/(LF + HF)
- HFnu = HF/(LF + HF)
- LFHF Ratio - Low frequency and high frequency ratio.
- ErHF - Renyi entropy – High frequency.
- ErLF - Renyi entropy – Low frequency.
- ErLHF - Renyi entropy – Low & high frequency ratio.
- ErO - Renyi entropy – Overall.
- EsHF - Shannon entropy – High frequency.
- EsLF - Shannon entropy – Low frequency.
- EsLFHFr - Shannon entropy – Low & high frequency ratio.
- EsO - Shannon entropy – Overall.
- VLF, LF, HF, EsHF, EsLFHFr, ErHF, ErO
- VLF, LF, HF

In addition, K-Folds Cross Validation and Leave One Out (LOO) Cross Validation were tested in order to identify the optimum cross validation method. For classification evaluation, a confusion matrix was used to calculate the accuracy (Eq. 1), sensitivity (Eq. 2) and specificity (Eq. 3), as illustrated below in Fig. 1. All the computations were done using MATLAB software.

		Predicted Class	
		0	1
True Class	0	True Negative (TN)	False Positive (FP)
	1	False Negative (FN)	True Positive (TP)

Fig. 1 - Confusion Matrix (0: Normal; 1: Autism)

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN} \quad (1)$$

$$\text{Sensitivity} = \frac{TP}{TP + FN} \quad (2)$$

$$\text{Specificity} = \frac{TN}{TN + FP} \quad (3)$$

3. Results and Discussion

3.1 Cross Validation

Table 1 and Table 2 show the performance of the LOO cross validation and 5-fold cross validation for all 19 HRV features, respectively. The LOO cross validation method was followed by setting the k-fold number to the number of samples used in this project (10 samples). The result showed a consistent performance for all the attempts, parameters and models, unlike the 5-Fold cross validation method. The 5-Fold cross validation method might result in higher accuracy in some cases, but its performance has been proven to be biased and is expected to be false or inaccurate based on a repetition of attempts for the same parameters. It is expected that this accuracy percentage is based on the samples

that had been collected together as a fold or a block, which changes randomly every time the dataset is loaded and divided. This would be an undesirable outcome as this study continued to change more parameters, whereby consistent and unbiased results were expected in each repetition and/or iteration.

Table 1 - Performance of 10-fold (LOO) cross validation for 19 Features

Number of attempts	Models								
	Logistic Regression			Linear Discriminant			Cubic SVM		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1st attempt	**50**	60	40	**40**	40	40	**60**	100	20
2nd attempt	**50**	60	40	**40**	40	40	**60**	100	20
3rd attempt	**50**	60	40	**40**	40	40	**60**	100	20

Table 2 - Performance of 5-fold cross validation for 19 Features

Number of attempts	Models								
	Logistic Regression			Linear Discriminant			Cubic SVM		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
1st attempt	**50**	80	20	**30**	40	20	**60**	100	20
2nd attempt	**60**	60	60	**60**	40	80	**60**	80	40
3rd attempt	**60**	80	40	**60**	60	60	**60**	100	20

3.2 Baseline Test Machine Learning Model

Table 3 shows the performance of three different forms of machine learning using the baseline test dataset. From the table, it can be seen that cubic SVM had the highest accuracy (60%) in all 19 features compared to the other two models. However, to decrease the data dimensionality and computational cost, and to optimise the performance, fewer features were proposed. From the result (Table 3), the accuracy of Logistic Regression and Linear Discriminant Analysis increased with the reduction of the number of features used, but this was not the case for the cubic SVM. The accuracy, sensitivity and specificity of Logistic Regression and Linear Discriminant Analysis with the second feature combinations (VLF, LF, HF, EsHF, EsLFHFr, ErHF, ErO) were the same, at 70%, 100% and 40% respectively. With the third feature combination (VLF, LF, HF), Linear Discriminant Analysis performed with better accuracy (90%) than Logistic Regression. Therefore, the Linear Discriminant model with the VLF, LF and HF features combination was found to be the best approach to distinguish between normal and autistic children during resting conditions / baseline.

Table 3 - Performance (accuracy) of different feature combinations in the Baseline Test

Features Combination	Models								
	Logistic Regression			Linear Discriminant			Cubic SVM		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
All 19 features	**50**	60	40	**40**	60	40	**60**	100	20
vlf, lf, hf, EsHF, EsLFHFr, ErHF, ErO	**70**	100	40	**70**	100	40	**50**	100	0
VLF, LF, HF	**80**	80	80	**90**	100	80	**40**	40	40

3.3 Colour Test Machine Learning Model

Table 4 shows the performance of three different forms of machine learning for the colour test. It was observed that accuracy, sensitivity and specificity were higher using the features combination of (VLF, LF, HF, EsHF, EsLFHFr, ErHF, ErO) than when using all 19 features or a combination of (VLF, LF, HF) for the classification. For the classifier performance, Logistic Regression and Linear Discriminant Analysis performed with higher accuracy than Cubic SVM. The training time was affected by the number of features being used for classification. The more features being used, the longer the necessary training time. Although the features combination of (VLF, LF, HF) took the shortest training time, the resulting accuracy was found to be much lower compared to the other two combinations. Using Logistic Regression with the feature's combination of (VLF, LF, HF, EsHF, EsLFHFr, ErHF, ErO), as extracted from the HRV signal (colour test), the highest accuracy, sensitivity and specificity were achieved, which were all 100%.

Table 4 - Performance (accuracy) of different feature combinations for Colour Stimulus Test

Features Combination	Models								
	Logistic Regression			Linear Discriminant			Cubic SVM		
	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Sensitivity (%)	Specificity (%)
All 19 features	**70**	100	40	**80**	100	60	**50**	80	20
VLF, LF, HF, EsHF, EsLFHFr, ErHF, ErO	**100**	100	100	**90**	100	80	**60**	80	40
VLF, LF, HF	**50**	40	60	**50**	40	60	**40**	20	60

4. Conclusion

ASD is a developmental disorder involving early childhood communication difficulties, as well as behavioural and social functioning problems. Early diagnosis is important to allow ASD patients to receive early treatment, which is essential for their growth development. Assessing the ANS is one of the early diagnostic strategies. PPG is a preferable method of measuring HRV, which is one of the most valuable markers of ANS due to its simplicity, lightness and wearability, as well as its ability to be applied at the peripheral position. Ten-fold cross-validation was selected for assessing the effectiveness of models because it gives high variations in the testing and training data, reduces bias and gives consistent results for all the attempts, parameters and models. Logistic Regression, Linear Discriminant Analysis and Cubic SVM were the three best classifiers chosen and the study evaluated their performance (accuracy) in differentiating between normal and autistic children. Three different combinations of features were proposed: all 19 features; a combination of VLF, LF, HF, EsHF, EsLFHFr, ErHF and ErO, and a combination of VLF, LF and HF. A confusion matrix was used to further evaluate each classifier's performance with different feature combinations by showing the sensitivity and specificity of each combination. The results showed that Logistic Regression is the best classifier for differentiating between autistic and normal children in a colour stimulus test, with its accuracy rating of 100%. Meanwhile, Linear Discriminant Analysis is best suited to the baseline test, with an accuracy rating of 90%. Even though the colour test gave better accuracy, the baseline test is recommended due to the consideration of computational and clinical resources. The results revealed that a machine learning approach could be an alternative method of making early diagnoses of ASD in the near future.

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References

[1] Ornoy, A., Weinstein-Fudim, L., & Ergaz, Z. (2015). Prenatal factors associated with autism spectrum disorder (ASD). Reproductive Toxicology, 56, 155–169.

[2] Mohd, M. S., Aimie-Salleh, N., Wahab, A. H. A., Sahalan, M., & Ashari, U. M. M. (2020). Heart rate variability response on autism spectrum disorder and typical development children, 4th International Symposium on Multidisciplinary Studies and Innovative Technologies. Istanbul, Turkey, 1–3.

[3] Raj, S., & Masood, S. (2020). Analysis and detection of autism spectrum disorder using machine learning techniques. Procedia Computer Science, 167, 994–1004.

[4] Kamal, A. (2016). Assessment of autonomic function in children with autism and normal children using spectral analysis and posture entrainment: A pilot study. Journal of Neurology and Neuroscience, 6(3), 1–5.

[5] Shihab, I. (2018). Classification and monitoring of autism using SVM and VMCM. Journal of Theoretical and Applied Information Technology, 96(14), 4379–4389.

[6] Nair, B. J. B., Shobha, R. N., Saikrishna, S. & Adith, C. (2019), Experiment to classify autism through brain MRI analysis. International Journal of Recent Technology and Engineering, 8(1S4), 383–386.

[7] Olaniyan, O., Oyedeji, A., & Ifeka, O. (2021). Development of a microcontroller EEG-based system for diagnosis of autism spectrum disorder in developing countries. International Conference on Recent Trends in Applied Research. Nigeria, 1–10.

[8] Song, R., Liu, J., & Kong, X. (2016). Autonomic dysfunction and autism: subtypes and clinical perspectives. North American Journal of Medicine and Science, 9(4), 172–180.

[9] Schaaf, R. C., Benevides, T. W., Leiby, B. E., & Sendecki, J. A. (2013). Autonomic dysregulation during sensory stimulation in children with autism spectrum disorder. Journal of Autism and Developmental Disorders, 45(2), 461–472.

[10] Acharya, U. R., Joseph, K. P., Kannathal, N., Lim, C. M., & Suri, J. S. (2006). Heart rate variability: A review. Medical and Biological Engineering and Computing, 44(12), 1031–1051.
[11] Porges, S. W. (2007). The polyvagal perspective. Biological Psychology, 74(2), 116–143.
[12] Bazelmans, T., Jones, E. J. H., Ghods, S., Corrigan, S., Toth, K., Charman, T., & Webb, S. J. (2019). Heart rate mean and variability as a biomarker for phenotypic variation in preschoolers with autism spectrum disorder. Autism Research, 12(1), 39–52.
[13] Rogers, S. J., Vismara, L., Wagner, A. L., McCormick, C., Young, G., & Ozonoff, S. (2014). Autism treatment in the first year of life: A pilot study of infant start, a parent-implemented intervention for symptomatic infants. Journal of Autism and Developmental Disorders, 44(12), 2981–2995.
[14] Tessier, M. P., Pennestri, M. H., & Godbout, R. (2018). Heart rate variability of typically developing and autistic children and adults before, during and after sleep. International Journal of Psychophysiology, 134, 15–21.
[15] Toichi, M. and Kamio, Y. (2003). Paradoxical autonomic response to mental tasks in autism. Journal of Autism and Developmental Disorders, 33(4), 417–426.
[16] Kleiger, R. E., Bigger, J. T., Bosner, M. S., Chung, M. K., Cook, J. R., Rolnitzky, L. M., Steinman, R., & Fleiss, J. L. (1991). Stability over time of variables measuring heart rate variability in normal subjects. The American Journal of Cardiology, 68(6), 626–630.
[17] Lan, K. C., Raknim, P., Kao, W. F., & Huang, J. H. (2018). Toward hypertension prediction based on PPG-derived HRV signals: A feasibility study. Journal of Medical Systems, 42(6), 1–7.
[18] Bujnakova, I., Ondrejka, I., Mestanik, M., Visnovcova, Z., Mestanikova, A., Hrtanek, I., Fleskova, D., Calkovska, A., & Tonhajzerova, I. (2016). Autism spectrum disorder is associated with autonomic underarousal. Physiological Research, 65(5), S673–S682.
[19] Nitzan, M., Babchenko, A., Khanokh, B., & Landau, D. (1998). The variability of the photoplethysmographic signal: A potential method for the evaluation of the autonomic nervous system. Physiological Measurement, 19(1), 93–102.
[20] Nitzan, M., Turivnenko, S., Milston, A., Babchenko, A., & Mahler, Y. (1996). Low- frequency variability in the blood volume and in the blood volume pulse measured by photoplethysmography. Journal of Biomedical Optics, 1(2), 223–229.
[21] Bazelmans, T., Jones, E. J., Ghods, S., Corrigan, S., Toth, K., Charman, T., & Webb, S. J. (2019). Heart rate mean and variability as a biomarker for phenotypic variation in preschoolers with autism spectrum disorder. Autism Research, 12(1), 39–52.