Developing a reliable and practical multi-domain model to facilitate the diagnosis of ADHD in older preschool children

I-Chun Chen (cyc@tmu.edu.tw)
Ton-Yen General Hospital
Che-Lun Chang
Artise Biomedical Co., Ltd
Meng-Han Chang
Ton-Yen General Hospital
Li-Wei Ko
National Yang Ming Chiao Tung University

Research Article

Keywords: attention-deficit/hyperactivity disorders (ADHD), preschool children, EEG, Conners' Kiddie Continuous Performance Test (K-CPT), rating scales, artificial intelligence (AI)

Posted Date: January 30th, 2024

DOI: https://doi.org/10.21203/rs.3.rs-3896489/v1

Additional Declarations: No competing interests reported.

Abstract

A multi-method, multi-informant approach is emphasized for the evaluations of attention-deficit/hyperactivity disorders (ADHD) in preschool children due to the complexity and challenges of diagnosis at this stage. Most artificial intelligence (AI) studies on the automated detection of ADHD used a single type of data. This study aims to create a reliable multimodal AI-detection system for facilitating the diagnosis of ADHD among older preschool children. 78 older preschool children were recruited; 43 (mean age: 68.07 ± 6.19 months) of them were diagnosed with ADHD and 35 (mean age: 67.40 ± 5.44 months) of them were with typical development (TD). Machine learning (ML) and deep learning (DL) methods were adopted to develop three individual predictive models by using electroencephalography (EEG) data recording with a wearable wireless device, scores of the computerized attention assessment via Conners' Kiddie Continuous Performance Test (K-CPT), and ratings of the ADHD-related symptom scales; finally, one ensemble model was merged. The results suggest that teacher ratings, K-CPT reaction time, and occipital high-frequency EEG band power values are significant features in identifying older preschool children with ADHD, and the ensemble model can achieve an accuracy of 0.974. The present study can respond to the three issues in most ADHD-related AI studies: the utility of wearable technologies, databases derived from different types of ADHD diagnostic instruments, and appropriate interpretability of the models. This established multimodal system can be reliable and practical in discriminating ADHD from TD and further facilitate the clinical diagnosis of preschool ADHD.

Introduction

Artificial intelligence (AI) and machine learning (ML)-based approaches to analyze medical information and biological signals have developed progressively in recent decades. In the clinical research regarding neurodevelopmental disorders, neuroscientists have made efforts to survey the brain-mind-behavioral relationship via the AI and ML technique pertaining to the neurobiological features of the brain [1]. Among multimodal data such as genetic, neuroimaging, and clinical behavioral data, electroencephalography (EEG) recording is non-invasive, easy to implement, inexpensive, more tolerant of motion artifacts recording, and excellent in temporal resolution [2–5]. The aforementioned advantages facilitate the study of infants and young children, particularly the neural activity during cognitive processing, which is the most challenging for investigation.

Attention-Deficit/Hyperactivity Disorder (ADHD) is an early-onset neurobehavioral disorder and can apparently influence children's learning, social performance, and well-being from preschool age [6–8]; the American Academy of Pediatrics, "Clinical Practice Guideline: Diagnosis and Evaluation of the Child with ADHD" has addressed the evaluation, diagnosis, and treatment of ADHD in children from age 4 to 18 years [8]. The diagnosis standard of ADHD in preschool children requires that the core symptoms present across more than one setting, which may be problematic to judge when the child does not undergo care or education outside the home [9]. Normally, this information is obtained from clinical interviews with parents, direct observation of the patient in the clinical setting, and symptom characteristics checklists from two circumstances. Neuropsychological measures may be used to support the clinical diagnosis

[10]. The same as school-age children, a multi-method, multi-informant approach that evaluates behavioral functioning across multiple settings is emphasized for the evaluation and diagnosis of ADHD in preschoolers [9, 11].

Due to the complexity and challenges of ADHD diagnosis, numerous studies considered other pathways to improve the efficiency of early diagnosis by using AI techniques, namely ML and deep learning (DL) methodologies to establish and promote the accuracy of ADHD diagnosis. In the review of AI studies of ADHD [12], the authors indicated this research lacked focus on the utility of wearable technologies for ADHD diagnosis and proposed AI should be extended to multiple types of datasets derived from diagnostic instruments, which enable the establishment of a robust clinical judgment assistive scheme regarding ADHD both in and out of the clinical settings.

Most AI studies on the automated detection of ADHD used a single type of data such as MRI, EEG, questionnaires, game-based tests, etc.…. To the best of our knowledge, few studies target preschool children and use multiple modalities to develop their models although some recent studies started trying to combine more than one evaluation tool to establish an AI-assisted diagnosis system regarding ADHD [13–16]. Since the 'gold standard' of diagnosing ADHD is highly recommended to comprise a combination of neuropsychological tests, behavioral rating scales from different observers, clinical interviews, and examination of the prognosis of interventions; a multi-method, multi-informant approach that evaluates manifestation functioning across more than one settings is optimal for the assessment of ADHD in preschoolers [11, 17]. One single modality AI approach for ADHD diagnosis has been surveyed widely in the past, however, a multimodal method may be more appropriate due to the heterogeneous clinical properties of ADHD.

The aim of this study is to respond to the aforementioned issues by using a wearable wireless EEG device combined with standard diagnostic tools via the continuous performance test (CPT) and the ADHD-related symptom scoring inventory to create a reliable AI-detection system. We assumed this multimodal system could be a practical, powerful, and clinically explainable scheme for assisting the diagnosis of ADHD at the preschool age.

Materials and methods

Participants

This study enrolled a total of 78 older preschool children; these children were not yet in primary school at the time of their participation in the experiment, and they were all kindergarten children. Of these, 43 of them were diagnosed with ADHD (35 boys, mean age: 68.07 ± 6.19 months) and 35 of them were with typical development (TD) (25 boys, mean age: 67.40 ± 5.44 months). This sample did not include children with significant neurological disorders, congenital syndromes, chromosomal and genetic disorders, hearing or visual impairments, autism spectrum disorders, mental retardation, or any other psychiatric disorders. All participants with ADHD were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-V) [6] criteria by the certified child and adolescent psychiatrist in the clinical setting.

All participating children and parents were informed with details regarding the experiment by the project leader of the study, and written informed consent was obtained from the parents before their recruitment into the study. The study protocol was approved by the Research Ethics Committee of the National Health Research Institutes in Taiwan (EC1070401-F).

Clinical neuropsychological measurement

Intelligence test and ADHD-related behavioral rating scales

The Taiwanese version of the Wechsler Preschool and Primary Scale of Intelligence, Fourth Edition was used to evaluate all participating children's cognitive functioning by qualified psychologists in the clinical setting [18]. To assess ADHD symptoms in all subjects, two versions of the Disruptive Behavior Disorder Rating Scale (DBDRS), designed for parents and teachers, were completed by the subjects' parents and kindergarten teachers. The DBDRS includes two major ADHD-related dimensions (a. inattention and b. hyperactivity-impulsivity) and is appropriate for use with older preschool children [19]. The DBDRS has been shown to be reliable and valid in preschool children across a variety of study samples [20, 21].

Conners' Kiddie Continuous Performance Test, Second Edition.

The commercially available computerized instrument, Conners' Kiddie Continuous Performance Test Second Edition (K-CPT-2) [22], was used to assess the attention-related performance of the children who participated in this study. The KCPT-2 incorporated five blocks (sets of trials), and one block consisted of two sub-blocks; each sub-block included 20 trials. After a total of 200 trials, which took 7.5 minutes to complete, nine main standardized scores were generated to allow the clinician to interpret the children's attentional problems. As defined by a mean of 50 and a SD of 10, higher scores indicate poorer performance, with the exception of hit reaction time (HRT).

In these main indices, d' (detectability) estimates the ability to discriminate between targets and non-targets. Omissions represent the rate of missed targets, and commissions represent the rate of incorrect responses to nontargets. Perseverations refer to anticipatory, repetitive, or random responses detected in less than 100 ms after the stimulus. HRT calculates the mean response speed of all non-perseverative responses for the entire test. HRT SD and variability indicate the consistency of the response speed. HRT Block Change indicates sustained attention ability by calculating the slopes of change in reaction time over five blocks of administration, and HRT Inter-stimulus Interval (ISI) Change measures the slope of change in reaction time between two ISIs (longer or shorter) and indicates the vigilance performance of subjects [22].

Experimental paradigm (Fig. 1)

In the experimental procedure, the participating children were instructed to sit on a steady seat in front of a computer screen. The assessor persuaded the children to relax, made sure they felt comfortable, and then recorded one minute of baseline eye open (EO) resting EEG data. Next, the assessor provided the test instructions and guided the children to practice before the required test. Finally, task EEG data was recorded during the formal K-CPT for 7.5 minutes after practice [23–26].

EEG recording via wearable technology (Fig. 1)

In this study, a wearable wireless 8-channel system [25, 27] (Mindo BR8, the Brain Research Center of National Chiao Tung University, Hsinchu, Taiwan) was applied to receive the EEG data (one-minute EO resting and 7.5 minutes task) from all participating children. The raw EEG signal was received from eight electrode sites on the scalp (Fp1, Fp2, Fz, C3, C4, Pz, O1, and O2). The impedance was set below 100 κOhms; the EEG data was recorded at a rate of 1000 samples per second and referenced to linked earlobes [25, 27]. This comfortable and easy-to-use device has been shown to be highly applicable for clinical use in young children [23–25].

EEG Signals Processing (Fig. 1)

Artefact removal

To improve signal quality, the EEG experts in the study used two approaches [23–25]. First, the raw signal was filtered using basic FIR filters (0.5–50 Hz); then all trials were visually inspected and segments containing electrical, muscular, or eye movement artifacts were identified and manually rejected using Independent Component Analysis (ICA). ICA is a widely used blind source separation method and can divide multivariate signals into those in the region of interest and those with artifacts [28]. Since the defective components related to artifacts were eliminated after the ICA treatment, the remaining components were back-projected and these artifact-free data were used for further analysis.

Datasets for input

According to the conditions of data recording, one minute of resting power and 7.5 minutes of the task, namely K-CPT power, were separately inputted for further computation.

Fast Fourier Transform (FFT)

To convert the raw time domain signal into the frequency band domains ranging from 0–50 Hertz (Hz), the Welch function of FFT was adopted in this study. Five different frequency bands were defined as follows: delta (1–4 Hz), theta (4–8 Hz), alpha (8–13 Hz), beta (13–30 Hz), and low gamma (30–50) band.

Normalization of the input data

Min-max normalization was applied to the absolute power of data.

EEG-based classification model to identify ADHD

Deep learning model

To explore the most optimal model for analyzing the data, bidirectional LSTM (Long Short-Term Memory) was implemented, which is a type of recurrent neural network architecture that extends the traditional LSTM model by processing input sequences in both forward and backward directions. In a regular LSTM, information flows from the past to the future, sequentially processing the input sequence. However, a bidirectional LSTM allows the network to capture dependencies from both past and future contexts [29].

The bidirectional LSTM consists of two LSTM layers: one processes the input sequence from left to right (forward LSTM), and the other processes the sequence in the reverse direction (backward LSTM). Each LSTM layer contains multiple memory cells or units that maintain a hidden state representing the previous information seen in the sequence. These hidden states are updated based on the current input and the previous hidden state using a set of learned weights.

After processing the input sequence in both directions, the output of the bidirectional LSTM is typically obtained by concatenating the forward and backward hidden states at each time step. This combined representation captures information from both past and future contexts and can be used for further tasks such as classification, sequence labeling, or sequence generation.

Bidirectional LSTMs are particularly useful in tasks where the current prediction depends on not only the past but also future context, such as natural language processing tasks like machine translation, sentiment analysis, speech recognition, and named entity recognition. By leveraging both forward and backward information, bidirectional LSTMs enhance the model's ability to capture complex patterns and dependencies in sequential data.

In this present study, the EEG datasets of each participating child are analyzed separately since the proposed LSTM network is trained to identify ADHD in a patient-specific approach. The EEG features used for signal analysis are extracted from every 0.001-sec long EEG segment (i.e. 60,000 resting and 450,000 task EEG data samples) to be used as input to the LSTM classifier. (Supplementary Fig. 1)

Hyperparameter tuning

Based on the process of grid search for hyperparameter tuning, we selected the most optimal pattern as our training model with a hyperparameter setting. (Supplementary Fig. 2)

Validation method

To evaluate the quality of the predictive EEG-based model, we use 70% of the data as training and 30% as testing. In validation, we use 90% as training and 10% as validation.

The classifiers for neuropsychological measurement

Regarding clinical neuropsychological measures (DBDRS and K-CPT-2 scores), the decision tree (DT) and random forest (RF) classifiers were used for the study.

Performance evaluation and feature analysis of models

To evaluate the performance of the prediction models, we use precision, recall, and F1 score to display the result corresponding to the three individual and the ensemble model.

For clinical neuropsychological and EEG data, we want to clarify which features are most important for differentiation. Using permutation methods, we determined the ranks of important features from the inner loop in the individual models.

Ensemble of classifiers (Fig. 2)

To obtain a merging single classification system, we established an ensemble of classifiers by combining the diverse predictive models generated earlier. More specifically, we trained three different classifiers with independent datasets, and further derived three independent predictive models, namely the "Predictive model #1" trained on DBRS features, the "Predictive model #2" trained on K-CPT features, and the "Predictive model #3" trained on EEG features.

Figure 2 shows the ensemble model proposed in this research. The ensemble model consists of 3 basic classifiers, they are DT, RF and bidirectional LSTM model.

$$f_{(x)} = \frac{1}{3}x_1 + \frac{1}{3}x_2 + \frac{1}{3}x_3$$

Where, $f_{(x)}$is an aggregate function of the ensemble models, and x_1, x_2, x_3 are the predicted outputs for each model. In this experiment, we use the same weight for each model. To predict the target label class, we use an aggregator function where the threshold value is 0.5. If the value of $f_{(x)}$ is greater than 0.5 then the predicted value is 1, and vice versa.

$$\hat{y} = \begin{cases} 1, iff_{(x)} \geq 0.5 \\ 0, otherwise \end{cases}$$

Statistical analysis

Demographic and clinical measures were compared between the two groups using independent t-tests, and comparative analysis of categorical variables (e.g., sex) was performed using a chi-squared test.

Results

Demographic and clinical measurement data

Table 1 revealed the comparison of the demographic and clinical measurements between the two groups. There were no significant differences regarding the mean age, sex distribution, full-scale intelligence quotient, and the verbal comprehensive index between the two groups.

Table 1
Comparison of demographic characteristics and clinical measures for total sample, ADHD, and TD

Mean (SD)	ADHD	TD	P-value
	n = 43	n = 35	
Age-months	68.07 (6.19)	67.40 (5.44)	0.617
Gender (male/female)	35/8	25/10	0.418
FSIQ	94.49 (14.03)	96.45 (3.96)	0.546
VCI	98.05 (12.83)	96.79 (3.18)	0.676
DBDRS-P-i	13.86 (4.41)	9.57 (4.92)	< 0.001**
DBDRS-P-h	13.14 (5.90)	8.11(5.21)	< 0.001**
DBDRS-T-i	15.58 (5.18)	8.79 (6.07)	< 0.001**
DBDRS-T-h	13.35 (5.85)	6.71 (7.20)	< 0.001**
d'	51.74 (7.46)	48.77 (6.50)	0.068
Omission	51.09 (8.00)	48.09 (7.61)	0.096
Commission	50.16 (8.85)	47.66 (8.83)	0.217
Perseveration	49.07 (6.23)	47.83 (6.99)	0.41
HRT	58.28 (8.24)	55.17 (6.62)	0.075
HRT SD	52.05 (8.45)	47.94 (6.49)	0.021*
Variability	51.72 (9.51)	48.00 (6.49)	0.052
HRT block change	50.53 (8.51)	48.74 (5.63)	0.288
HRT ISI change	52.44 (8.89)	47.69 (8.62)	0.020*

** $P < 0.01$, * $P < 0.05$; ADHD: attention-deficit/hyperactivity disorder, TD: typical development, SD: standard deviation, FSIQ: full-scale intelligence quotient, VCI: verbal comprehension index, DBDRS-P-i: Disruptive Behavior Disorder Rating Scale parent version inattentiveness dimension, DBDRS-P-h: Disruptive Behavior Disorder Rating Scale parent version hyperactivity dimension, DBDRS-T-i: Disruptive Behavior Disorder Rating Scale teacher version inattentiveness dimension, DBDRS-T-h: Disruptive Behavior Disorder Rating Scale teacher version hyperactivity dimension, d’ detectability, HRT: hit reaction time, ISI: inter-stimulus interval.

In term of the clinical measurement, significant differences were observed in specific DBDRS and the K-CPT2 scores between two groups; the group with ADHD were rated higher scores than TD in DBDRS-inattentive dimension by both parents (13.86 ± 4.41 versus 9.57 ± 4.92, p < 0.001) and teachers (15.58 ± 5.18 versus 8.79 ± 6.07, p < 0.001) and DBDRS-hyperactive dimension by both parents (13.14 ± 5.90 versus 8.11 ± 5.21, p < 0.001) and teachers (13.35 ± 5.85 versus 6.71 ± 7.20, p < 0.001). In respect of the K-

CPT2, the group with ADHD underperformed (scoring higher) than TD in HRT SD (52.05 ± 8.45 versus 47.94 ± 6.49, $p = 0.021$) and HRT ISI change (52.44 ± 8.89 versus 47.69 ± 8.62, $p = 0.020$) (Table 1).

Performance evaluation of models

Supplementary Fig. 3 shows the training results of model 3 generated by EEG data. Our model can achieve a maximum training accuracy of 0.9472 (94.72%) and a maximum validation accuracy of 87.68%. Epochs are represented 10 times for each scale in supplementary Fig. 3, which means that our model achieves maximum and stable accuracy after 120 epochs. Furthermore, for the testing phase, we used 5-fold cross-validation to ensure the robustness of the results, we found that our model can achieve 0.95 (95%) of accuracy (Table 2).

Table 2
Performance evaluators of the ADHD and TD classification models

Model #	**Precision**	**Recall**	**F1-Score**	**Accuracy**
1. Decision Tree	0.912	0.909	0.909	0.909
2. Random Forest	0.923	0.922	0.922	0.922
3. Bi-Direct. LSTM	0.950	0.940	0.950	0.950
Ensemble Model				**0.974**

With respect to model 1 & 2, the precision, the recall and the F1 score are listed in Table 2.

Ensemble model performance

It is noteworthy that the accuracy of the final ensemble model is 0.974 (Table 2).

Significant features analysis

Figure 3a shows that the most important feature from the dataset of model #1 is DBRShT, which shows the effect of a decrease in precision of about 0.25 with about plus minus 0.05. DBRSiT follows with the effect of a decreased precision value of about 0.13 with about plus minus 0.01.

Figure 3b shows that the most important feature from model #2 is HRT, which has the effect of decreasing the precision value by about 0.12 with approximately plus minus 0.02. ISI change follows with the effect of decreasing the precision value by 0.06 with approximately plus minus 0.02. Block change follows in third place with the effect of decreasing precision by 0.05 with approximately plus minus 0.02. The rest of the feature values are shown in Fig. 3b.

Figure 3c shows that the most important features from the data set of model #3 are O2 low-gamma, O2 beta, and O2 alpha, which have the effect of decreasing the precision values around 0.14, 0.12, and 0.07, respectively, in order.

Discussion

This study combined behavioral scales, computerized attention tests, and wireless EEG data to create a multimodal system, which can provide clinicians with a reliable, diverse perspective, and clinically explainable scheme for assisting the diagnosis of ADHD at the older preschool age. In this ensemble model, the DBDRS provides a subjective observation summary within a period from main caregivers, the K-CPT scores provide objective behavioral quantification, and the EEG recording indicates brain signals related to attention. These three dimensions of datasets represent different aspects of assessment approaches, which are consistent with the clinical guideline of multi-methods regarding preschool ADHD diagnosis. Our results can answer the three objectives in most ADHD-related AI studies: usability of wearable technologies, databases derived from different types of ADHD diagnostic instruments, and adequate interpretability of our ML and DL models.

Among numerous ADHD-related research, in the neuroimaging category, brain MRI data are mainly used to develop the AI models [1, 12]; in terms of physiological signals, EEG is the most widely studied instrument for surveying automated ADHD diagnostic systems, which also had favorable performances (accuracy results above 80–90% via ML or DL) [30–40]. Other biological data have attempted to identify genetic biomarkers of ADHD using methods of ML and DL [12]. Externalizing symptom and behavior measures using survey forms [41], performance tests [42], or motion data [43] were studied regarding ADHD classification among children. In general, all these studies focus on a single form of dataset; however, it's well known that the diagnosis of preschool ADHD should be based on multiple assessment approaches.

Few in the literature have made efforts to incorporate multiple data sets from different modalities [13–15]; Crippa et al. [13] investigated the capability of multi-domain profiles including blood fatty acid testing, neuropsychological assessments, and near-infrared spectroscopy measures, to correctly identify school-aged children with ADHD. Two studies by Yoo et al. [15] and Kautzky et al. [14] analyzed neuroimaging and genetic data to propose multivariate classification models for ADHD and healthy controls. Due to the invasive nature of blood testing and the less naturalistic experimental setting of MRI, these procedures may raise concerns about clinical practicality and compliance in preschool children. The present study overcomes these drawbacks by using the wireless EEG-integrated game-like test.

In our results, significant features from 3 different models consisted of scores of DBDRS rated by teachers and HRT in K-CPT, as well as EEG O2 low-gamma band power; these findings are clinically interpretable and compatible with previous literature. Tandon & Pergjika [44] indicated an increased judgment confidence in the improper behaviors of preschoolers if teachers reported the presence of symptoms. Rather than parents' feedback, the children in the present study were all educated in kindergarten, where the teacher can make more accurate comparisons with their peers without ADHD-related behaviors and then provide more valuable information. The results of our model #1 are compatible with previous literature supporting that teacher ratings may be superior to parent ratings [45, 46]. Regarding the reaction time, children with ADHD are typically less accurate, slower, and have more variable reaction times compared to their age-matched peers in the review articles [47, 48]. The results of our model #2 are consistent with this finding, indicating that HRT is the most significant feature.

The EEG feature analysis in model #3 observed that the resting band power of low-gamma and beta are the most important indicators. Most ADHD-related EEG literature has examined the power of theta and the theta-beta ratio [2, 3, 49–51]; few studies surveyed the gamma power for the small amplitude, and the importance of high-frequency EEG oscillations in cognitive function and neurodevelopmental disorders is often underestimated compared to low-frequency oscillations [52, 53]. Herrmann and Demiralp [52] mentioned that the hyperactive behavior of ADHD patients results from a neuronal hyper-excitation reflected by enhanced gamma activity. In terms of beta power, Clarke et al. [54, 55] found that a subgroup of children with ADHD had significantly excessive beta oscillations and they were further determined to be the combined type of ADHD in boys than girls. In the same cases with gamma response, this EEG profile of excess beta activity was viewed as hyper-arousal. Our results in feature analysis can be in line with previous conclusions. Additionally, to interpret the context of resting condition and occipital brain region, we speculated that it's related to the eye open and visual stimulation status during the baseline of the experiment.

We have tried to make the features of our predictive models well-explainable since the process of ML and DL algorithm is so complex, and clinicians usually consider these models like a “black box”, which is difficult to comprehend and utilize. In case of some variations of biomarkers and features existing between investigations of studies, it should be realized that these approaches used for establishing the AI models are multivariate analysis methods, and can offer the profits of identifying complicated patterns of differences that univariate statistical methods cannot efficiently differentiate [13].

In this present study, wearable technology is employed to record the biological signal; rather than the lengthy procedure of preparing traditional wet electrode EEG systems, the design of this device features convenience to use, which promotes the acceptance of some impatient and agitated children. Moreover, most of the child participants reacted comfortably and with little restraint during the measurements. In conclusion, this technology allows monitoring the brain dynamics of child subjects during task performance via enhancing cooperation and naturalistic situations, and we proposed that this wireless semidry-electrode EEG recording system can be appropriate as a data acquisition device, especially for young children; furthermore, to establish a robust AI-facilitating clinical decision system to identify ADHD both in and out of clinical settings.

Despite overcoming the challenge and difficulty of collecting task-related brain signals in young children, we analyzed the data of moderate sample size, there are some limitations regarding the present study. First, the relatively small sample size of the participating groups of children is still the main concern. Second, the findings of this work may be somewhat specific to the age group used in our sample (i.e., 5-7-year-old children with ADHD), so the present predictive models could not be extended and applied to all preschool children.

Conclusion

This present study is the scarce investigation focusing on older preschool children; a reliable model is established using non-invasive and wearable instruments to obtain multi-method datasets, and further reveals characteristic features for assisting ADHD diagnosis and interpreting underlying brain-behavior relationships. The findings suggest that teacher rating scores, HRT in K-CPT, and occipital high-frequency EEG band power are significant features to predict abnormality, and the ensemble model can achieve an accuracy of 0.974. In summary, this established multimodal system demonstrated the potential utility of multiple perspective assessment in discriminating ADHD from TD and explaining possible neural behavioral mechanisms associated with preschool ADHD.

Declarations

Acknowledgment

The authors express their sincere appreciation to all children and families who participated in this study and the assistance of Sheng Hong Precision Technology Co., Ltd.

Conflict of interest

The authors declare that they have no conflict of interest.

Author Contribution

IC Chen designed the experiment.IC Chen collected and analyzed the data.IC Chen wrote the manuscript under CL Chang's suggestions and supervision.MH Chang contributed to clinical diagnosis.LW KO contributed to general counselling.All authors contributed to the article and approved the submitted version

References

1. Gupta C et al (2022) Bringing machine learning to research on intellectual and developmental disabilities: taking inspiration from neurological diseases. J Neurodev Disord 14(1): p. 28. DOI: 10.1186/s11689-022-09438-w
2. Jeste SS, J. Frohlich J, Loo SK (2015) Electrophysiological biomarkers of diagnosis and outcome in neurodevelopmental disorders. Curr Opin Neurol 28(2): p. 110-6. doi: 10.1097/WCO.0000000000000181
3. Alba G et al (2015) Electroencephalography signatures of attention-deficit/hyperactivity disorder: clinical utility. Neuropsychiatric disease and treatment. 11: p. 2755-2769.DOI: 10.2147/NDT.S51783
4. McVoy M et al (2019) A systematic review of quantitative EEG as a possible biomarker in child psychiatric disorders. Psychiatry Res 279: p. 331-344. DOI: 10.1016/j.psychres.2019.07.004

5. Loo SK, Makeig S (2012) Clinical utility of EEG in attention-deficit/hyperactivity disorder: a research update. Neurotherapeutics. 9(3): p. 569-87. DOI: 10.1007/s13311-012-0131-z
6. American Psychiatric Association (2013), Diagnostic and Statistical Manual of Mental Disorders (DSM-5®). American Psychiatric Publishing.
7. Connor DF (2002) Preschool attention deficit hyperactivity disorder: a review of prevalence, diagnosis, neurobiology, and stimulant treatment. J Dev Behav Pediatr. 23(1 Suppl): p. S1-9. DOI: 10.1097/00004703-200202001-00002
8. Wolraich ML et al (2019) Clinical Practice Guideline for the Diagnosis, Evaluation, and Treatment of Attention-Deficit/Hyperactivity Disorder in Children and Adolescents. Pediatrics, 144(4): p. e20192528. doi: 10.1542/peds.2019-3997
9. Zaim N, Harrison J (2020) Pre-school mental health disorders: a review. International Review of Psychiatry 32(3): p. 189-201. doi: 10.1080/09540261.2019.1692793
10. Merkt J, Siniatchkin M, Petermann F (2020) Neuropsychological Measures in the Diagnosis of ADHD in Preschool: Can Developmental Research Inform Diagnostic Practice? J Atten Disord. 24(11): p. 1588-1604. DOI: 10.1177/1087054716629741
11. Halperin JM, Marks DJ (2019) Practitioner Review: Assessment and treatment of preschool children with attention-deficit/hyperactivity disorder. J Child Psychol Psychiatry DOI: 10.1111/jcpp.13014
12. Loh HW, et al (2022) Automated detection of ADHD: Current trends and future perspective. Comput Biol Med 146: p. 105525. DOI: 10.1016/j.compbiomed.2022.105525
13. Crippa A, et al (2017) The Utility of a Computerized Algorithm Based on a Multi-Domain Profile of Measures for the Diagnosis of Attention Deficit/Hyperactivity Disorder. Frontiers in Psychiatry 8. DOI: 10.3389/fpsyt.2017.00189
14. Kautzkyik A, et al (2020) Machine learning classification of ADHD and HC by multimodal serotonergic data. Translational Psychiatry 10(1): p. 104. DOI: 10.1038/s41398-020-0781-2
15. Yoo JH, et al. (2020) Exploring characteristic features of attention-deficit/hyperactivity disorder: findings from multi-modal MRI and candidate genetic data. Brain Imaging and Behavior 14(6): p. 2132-2147. DOI: 10.1007/s11682-019-00164-x
16. Muthuraman M, et al (2019) Multimodal alterations of directed connectivity profiles in patients with attention-deficit/hyperactivity disorders. Sci Rep 9(1): p. 20028. DOI: 10.1038/s41598-019-56398-8
17. Gualtieri CT, Johnson LG (2005) ADHD: Is Objective Diagnosis Possible? Psychiatry (Edgmont) 2(11): p. 44-53.
18. Chen J, Chen HT (2013) Taiwan: Chinese Behavioral Science Corporation, Manual for the Wechsler preschool and primary scale of intelligence-IV.
19. Barkley RA, Murphy KR(2005) Attention-deficit Hyperactivity Disorder: A Clinical Workbook.: Guilford Publications.
20. Friedman-Weieneth JL, et al (2008) The Disruptive Behavior Rating Scale—Parent Version (DBRS-PV): Factor Analytic Structure and Validity Among Young Preschool Children. Journal of Attention

Disorders. 13(1): p. 42-55. DOI: 10.1177/1087054708322991

21. Silva RR, et al (2005) A Rating Scale for Disruptive Behavior Disorders, Based on the DSM-IV Item Pool. Psychiatric Quarterly 76(4): p. 327-339. DOI: 10.1007/s11126-005-4966-x
22. Conners CNT (2015) NY: Multi-Health Systems Inc, Conners' Kiddie continuous performance test 2nd Edition.
23. Chen IC, et al (2022) Atypical functional connectivity during rest and task-related dynamic alteration in young children with attention deficit hyperactivity disorder: An analysis using the phase-locking value. Psychiatry and Clinical Neurosciences. DOI: 10.1111/pcn.13344
24. Chen IC, et al (2022) Task-Rate-Related Neural Dynamics Using Wireless EEG to Assist Diagnosis and Intervention Planning for Preschoolers with ADHD Exhibiting Heterogeneous Cognitive Proficiency. Journal of Personalized Medicine 12(5): p. 731. DOI: 10.3390/jpm12050731
25. Chen IC, et al (2021) Neural Dynamics for Facilitating ADHD Diagnosis in Preschoolers: Central and Parietal Delta Synchronization in the Kiddie Continuous Performance Test. IEEE Trans Neural Syst Rehabil Eng 29: p. 1524-1533. DOI: 10.1109/TNSRE.2021.3097551
26. Chen IC, et al (2022) Incremental Validity of Multi-Method and Multi-Informant Evaluations in the Clinical Diagnosis of Preschool ADHD. J Atten Disord 26(10): p. 1293-1303. DOI: 10.1177/10870547211045739
27. Ko LW, et al (2019) Development of a Smart Helmet for Strategical BCI Applications. Sensors (Basel) 19(8). DOI: 10.3390/s19081867
28. Pion-Tonachini L, Kreutz-Delgado K, Makeig S (2019) ICLabel: An automated electroencephalographic independent component classifier, dataset, and website. NeuroImage, 198: p. 181-197. DOI: 10.1016/j.dib.2019.104101
29. Graves A., Mohamed Ar, Hinton G (2013) Speech Recognition with Deep Recurrent Neural Networks. ICASSP, IEEE International Conference on Acoustics, Speech and Signal Processing - Proceedings 38. DOI:10.1109/ICASSP.2013.6638947
30. Öztoprak H, et al (2017) Machine-based classification of ADHD and nonADHD participants using time/frequency features of event-related neuroelectric activity. Clin Neurophysiol 128(12): p. 2400-2410. DOI: 10.1016/j.clinph.2017.09.105
31. Altınkaynak M, et al (2020) Diagnosis of Attention Deficit Hyperactivity Disorder with combined time and frequency features. Biocybernetics and Biomedical Engineering 40(3): p. 927-937. https://doi.org/10.1016/j.bbe.2020.04.006
32. Ahmadlou M, Adeli H (2010) Wavelet-Synchronization Methodology: A New Approach for EEG-Based Diagnosis of ADHD. Clinical EEG and Neuroscience 41(1): p. 1-10. DOI:10.1177/155005941004100103
33. Rezaeezadeh M, Shamekhi S, Shamsi M (2020) Attention Deficit Hyperactivity Disorder Diagnosis using non-linear univariate and multivariate EEG measurements: a preliminary study. Physical and Engineering Sciences in Medicine 43(2): p. 577-592. DOI: 10.1007/s13246-020-00858-3

34. Abibullaev B, An J (2012) Decision support algorithm for diagnosis of ADHD using electroencephalograms. J Med Syst 36(4): p. 2675-88. DOI: 10.1007/s10916-011-9742-x
35. Khoshnoud S, Nazari MA, Shamsi M (2018) Functional analysis of ADHD in children using nonlinear features of EEG signals. JIN 17(1): p. 11-18. DOI: 10.31083/JIN-170033
36. Chen H, Song Y, Li X (2019) Use of deep learning to detect personalized spatial-frequency abnormalities in EEGs of children with ADHD. J Neural Eng 16(6): p. 066046. DOI: 10.1088/1741-2552/ab3a0a
37. Moghaddari M, Lighvan MZ, Danishvar S (2020) Diagnose ADHD disorder in children using convolutional neural network based on continuous mental task EEG. Comput Methods Programs Biomed 197: p. 105738. DOI: 10.1016/j.cmpb.2020.105738
38. Tosun M (2021) Effects of spectral features of EEG signals recorded with different channels and recording statuses on ADHD classification with deep learning. Phys Eng Sci Med 44(3): p. 693-702. DOI: 10.1007/s13246-021-01018-x
39. Maya-Piedrahita MC (2022) Supported Diagnosis of Attention Deficit and Hyperactivity Disorder from EEG Based on Interpretable Kernels for Hidden Markov Models. Int J Neural Syst 32(3): p. 2250008. DOI: 10.1142/S0129065722500083
40. Wang C, et al (2022) Towards high-accuracy classifying attention-deficit/hyperactivity disorders using CNN-LSTM model. Journal of Neural Engineering. 19(4): p. 046015. DOI: 10.1088/1741-2552/ac7f5d
41. Öztekin I, et al (2021) Is there any incremental benefit to conducting neuroimaging and neurocognitive assessments in the diagnosis of ADHD in young children? A machine learning investigation. Developmental Cognitive Neuroscience. 49: p. 100966. DOI: 10.1016/j.dcn.2021.100966
42. Slobodin O, Yahav I, Berger I (2020) A Machine-Based Prediction Model of ADHD Using CPT Data. Frontiers in Human Neuroscience 14. DOI: 10.3389/fnhum.2020.560021
43. Amado-Caballero P, et al (2020) Objective ADHD Diagnosis Using Convolutional Neural Networks Over Daily-Life Activity Records. IEEE Journal of Biomedical and Health Informatics 24(9): p. 2690-2700. DOI: 10.1109/JBHI.2020.2964072
44. Tandon M, Pergjika A (2017) Attention Deficit Hyperactivity Disorder in Preschool-Age Children. Child Adolesc Psychiatr Clin N Am 26(3): p. 523-538. DOI: 10.1016/j.chc.2017.02.007
45. Power TJ, et al (1998) The Predictive Validity of Parent and Teacher Reports of ADHD Symptoms. Journal of Psychopathology and Behavioral Assessment 20(1): p. 57-81. DOI: 10.1023/A:1023035426642
46. Willcutt EG, et al (1999) Utility of behavior ratings by examiners during assessments of preschool children with attention-deficit/hyperactivity disorder. J Abnorm Child Psychol 27(6): p. 463-72. DOI: 10.1023/a:1021984126774
47. Karalunas SL, Huang-Pollock, CL, Nigg JT (2012) Decomposing attention-deficit/hyperactivity disorder (ADHD)-related effects in response speed and variability. Neuropsychology 26(6): p. 684-94.

. DOI: 10.1037/a0029936

48. Kofler MJ, et al (2013) Reaction time variability in ADHD: a meta-analytic review of 319 studies. Clin Psychol Rev 33(6): p. 795-811. DOI: 10.1016/j.cpr.2013.06.001
49. Lenartowicz A, Loo SK (2014) Use of EEG to diagnose ADHD. Curr Psychiatry Rep 16(11): p. 498. DOI: 10.1007/s11920-014-0498-0
50. Newson JJ, Thiagarajan TC (2018) EEG Frequency Bands in Psychiatric Disorders: A Review of Resting State Studies. Front Hum Neurosci 12: p. 521. DOI: 10.3389/fnhum.2018.00521
51. Clarke AR, Barry RJ, Johnstone S (2020) Resting state EEG power research in Attention-Deficit/Hyperactivity Disorder: A review update. Clin Neurophysiol 131(7): p. 1463-1479. DOI: 10.1016/j.clinph.2020.03.029
52. Herrmann CS, Demiralp T (2005) Human EEG gamma oscillations in neuropsychiatric disorders. Clinical Neurophysiology 116(12): p. 2719-2733. https://doi.org/10.1016/j.clinph.2005.07.007
53. Lenz D, et al (2008) Enhanced gamma-band activity in ADHD patients lacks correlation with memory performance found in healthy children. Brain Research 1235: p. 117-132. https://doi.org/10.1016/j.brainres.2008.06.023
54. Clarke AR, et al (2001) Excess beta activity in children with attention-deficit/hyperactivity disorder: an atypical electrophysiological group. Psychiatry Res 103(2-3): p. 205-18. DOI: 10.1016/s0165-1781(01)00277-3
55. Clarke AR, et al (2011) Behavioural differences between EEG-defined subgroups of children with Attention-Deficit/Hyperactivity Disorder. Clin Neurophysiol 122(7): p. 1333-41.

Figures

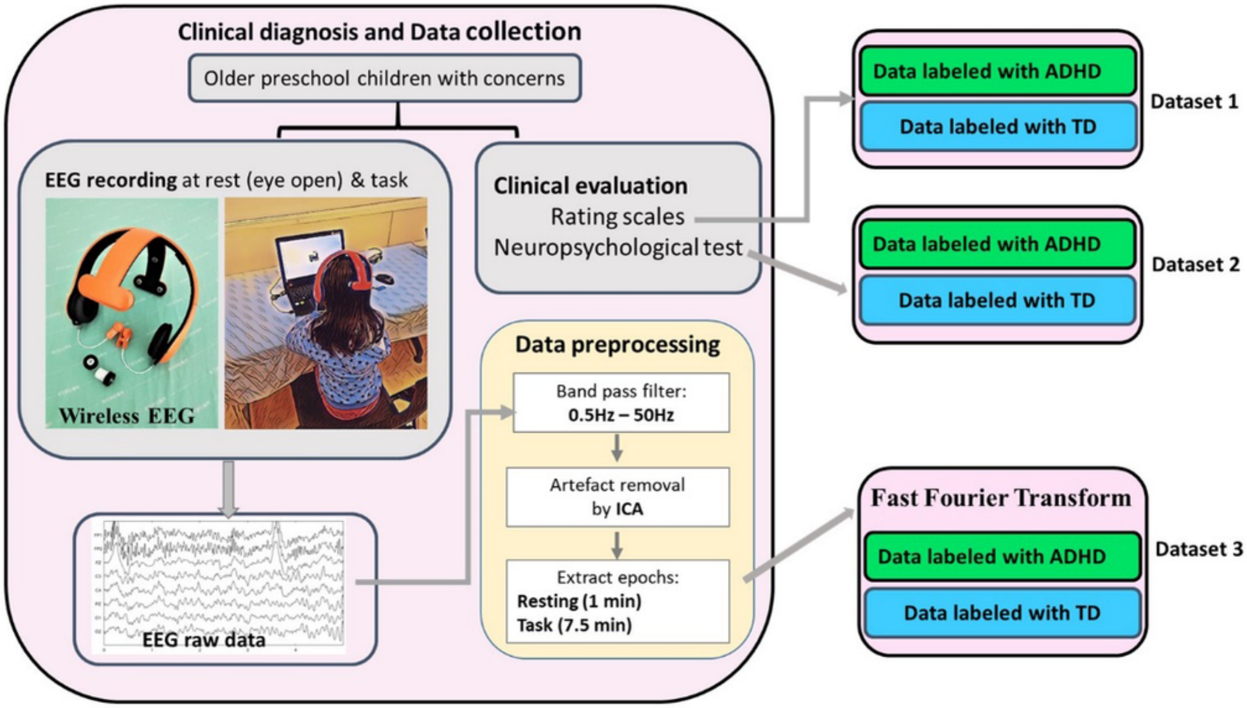

Figure 1

Graphical display of wireless EEG data collection and dataset generation.

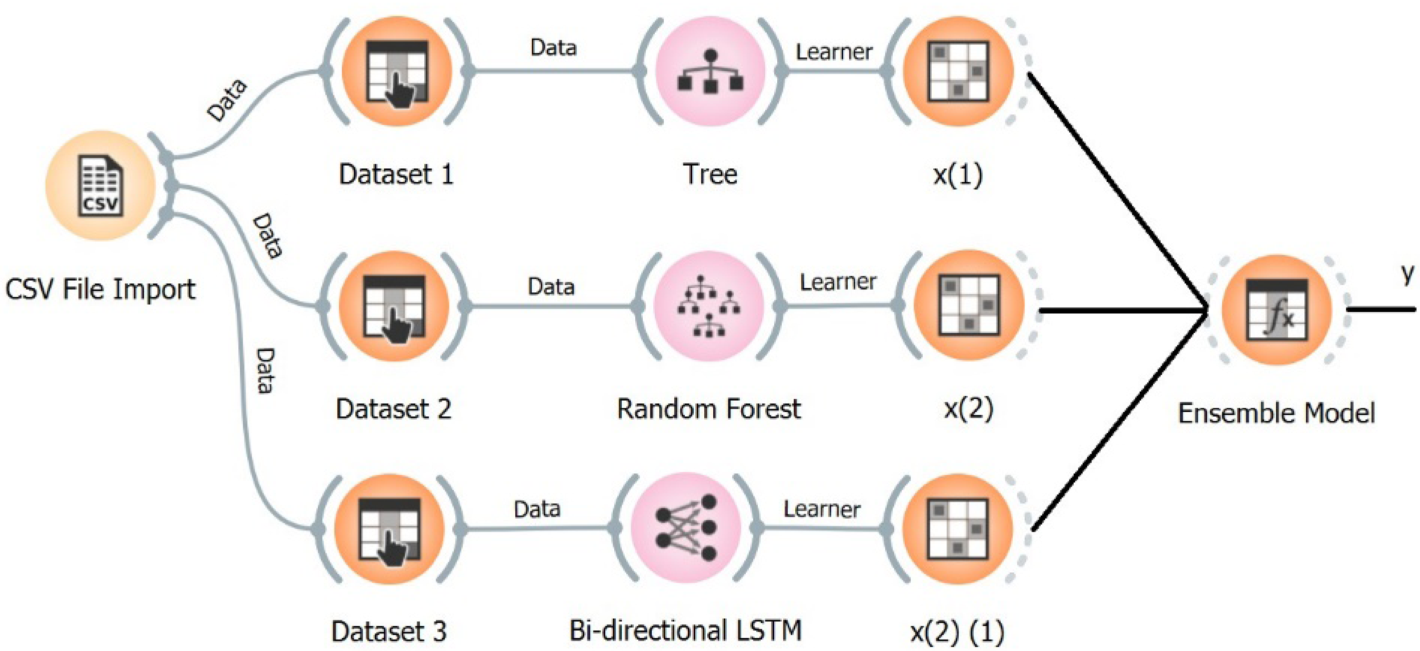

Figure 2

The ensemble model proposed in this research. The ensemble model consists of 3 basic classifiers: decision tree, random forest, and bidirectional LSTM models.

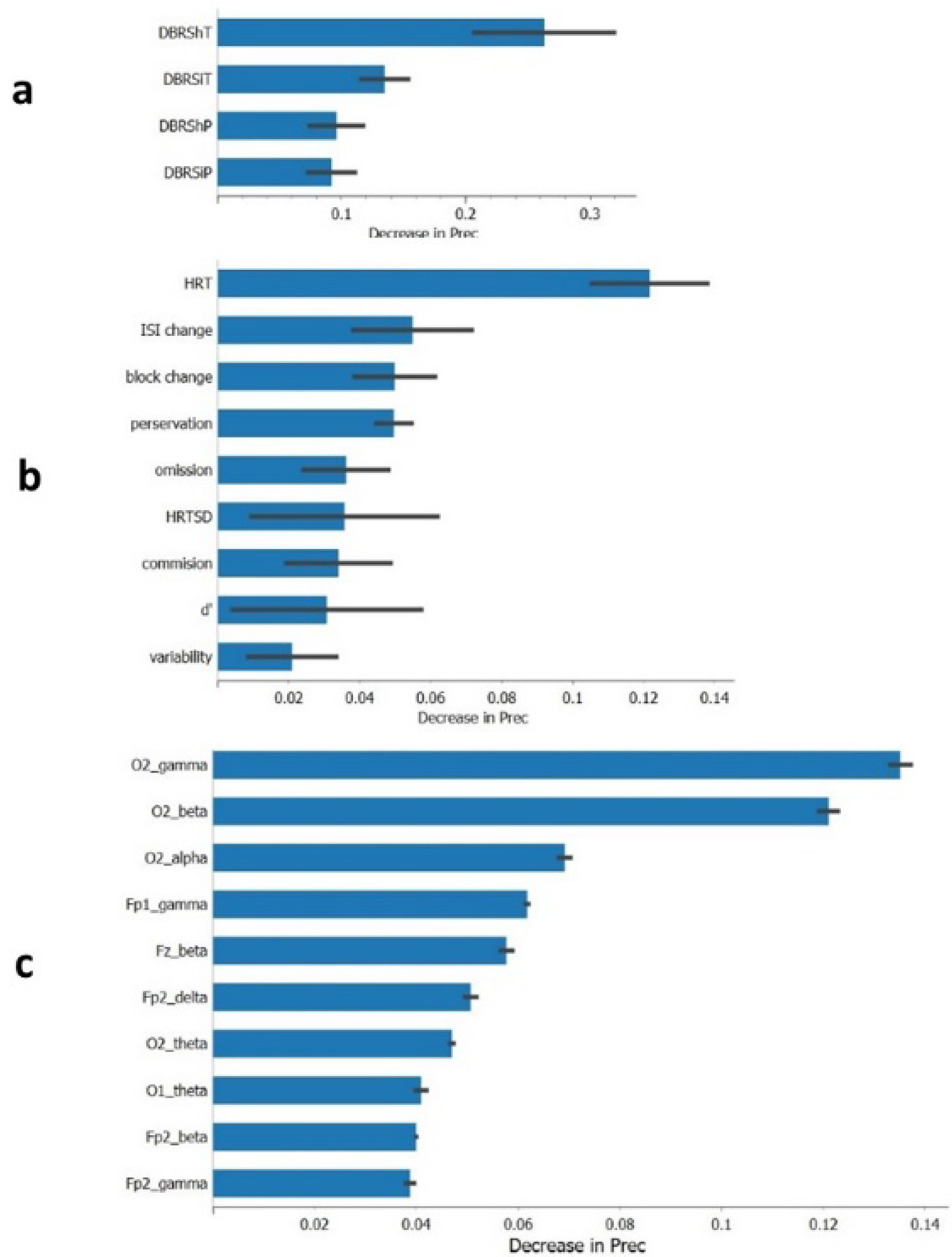

Figure 3

The ranks of important features in predictive model #1 - trained by decision tree (a), in predictive model #2 - trained by random forest (b), in predictive model #3 - trained by bidirectional LSTM.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupplementaryFigure.docx