ORIGINAL RESEARCH

Predicting Depression Among Chinese Patients with Narcolepsy Type 1: A Machine-Learning Approach

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Objective: Depression is a common psychiatric issue among patients with narcolepsy type 1 (NT1). Effective management requires accurate screening and prediction of depression in NT1 patients. This study aims to identify relevant factors for predicting depression in Chinese NT1 patients using machine learning (ML) approaches.

Methods: A total of 203 drug-free NT1 patients (aged 5–61), diagnosed based on the ICSD-3 criteria, were consecutively recruited from the Sleep Medicine Center at Peking University People's Hospital between September 2019 and April 2023. Depression, daytime sleepiness, and impulsivity were assessed using the Center for Epidemiologic Studies Depression Scale for Children (CES-DC) or the Self-Rating Depression Scale (SDS), the Epworth Sleepiness Scale for adult or children and adolescents (ESS or ESS-CHAD), and the Barratt Impulse Scale (BIS-11). Demographic characteristics and objective sleep parameters were also analyzed. Three ML models-Logistic Regression (LR), Random Forest (RF), and Support Vector Machine (SVM)-were used to predict depression. Model performance was evaluated using receiver operating curve (AUC), accuracy, precision, recall, F1 score, and decision curve analysis (DCA).

Results: The LR model identified hallucinations (OR 2.21, 95% CI 1.01–4.90, $p = 0.048$) and motor impulsivity (OR 1.10, 95% CI 1.02–1.18, $p = 0.015$) as predictors of depression. Among the ML models, SVM showed the best performance with an AUC of 0.653, accuracy of 0.659, sensitivity of 0.727, and F1 score of 0.696, reflecting its effectiveness in integrating sleep-related and psychosocial factors.

Conclusion: This study highlights the potential of ML models for predicting depression in NT1 patients. The SVM model shows promise in identifying patients at high risk of depression, offering a foundation for developing a data-driven, personalized decision-making tool. Further research should validate these findings in diverse populations and include additional psychological variables to enhance model accuracy.

Keywords: narcolepsy type 1, depression, machine learning, support vector machine

Introduction

Narcolepsy type 1 (NT1) is a specific subtype of narcolepsy, characterized by excessive daytime sleepiness (EDS), cataplexy, hypnagogic/hypnopompic hallucinations (HH), sleep paralysis (SP), and disrupted nocturnal sleep (DNS).[1] Importantly, neuropsychiatric manifestations are frequently observed in patients with narcolepsy.[2] Despite variations in the reported prevalence of psychiatric comorbidities among patients with narcolepsy, existing empirical evidence predominantly supports a higher incidence of depression compared to other psychiatric disorders.[3–6] For instance, research has shown that a higher proportion of patients with narcolepsy (32%, 95% Confidence Interval, 28–36%) experience depression or depressive symptoms.[7]

It has been confirmed that depression is associated with poor quality of life,[8,9] low physical activity levels[10] and decreased job effectiveness and daily activities[11] among patients with NT1. Furthermore, comorbid depression may increase the risk of suicidality in narcolepsy patients.[2] While depression is often overlooked and not adequately treated in patients with NT1. Research indicates that despite the high prevalence[7] and substantial effects of depression[9] in patients with narcolepsy, appropriate mental health care is not provided. European evidence-based guidelines[12] recommend treating psychiatric disorders in narcolepsy using general principles, as there are limited specific studies supporting any particular treatments for depression in narcolepsy. Only a few studies have explored non-pharmacological interventions, such as cognitive behavioral therapy (CBT)[13] and peer support,[14] to address the psychosocial needs of these patients. For example, Ong et al[13] developed a CBT for hypersomnia (CBT-H) program to address the psychosocial needs of individuals with central disorders of hypersomnolence (CDH), finding that it could reduce depressive symptoms (decrease in Patient Health Questionnaire ≥ 5) among patients with CDH. Consequently, early and accurate prediction of depression in patients with NT1 assumes paramount importance for disease management and enhancement of their overall well-being.

Several factors may contribute to the development of depression among patients with NT1, including neurobiological factors such as hypocretin deficit, cortisol levels, and corticotropin-releasing hormone (CRH) neurons;[15–17] sleep-related factors like sleep quality, EDS and hallucinations;[10,18] as well as psychosocial factors such as stigma or resilience.[19,20] As for neurobiological factors, the deficiency in hypocretin of cerebral spinal fluid (CSF) is believed to be a potential avenue for investigating the pathological basis of depression in patients with NT1.[16] Additionally, studies have demonstrated a reduction in CRH neurons in NT1,[21] accompanied by hyperactivity in the remaining neurons.[17] Given that paraventricular CRH neurons are crucial to the hypothalamic-pituitary-adrenal (HPA) stress axis and HPA axis overactivity is linked to depression,[22] this hyperactivity may significantly contribute to mood and anxiety symptoms in NT1. Moreover, it had been reported that the disruption of white matter integrity and prevalent brain degeneration of frontal lobes were associated with depressive symptoms in narcolepsy.[23] Concerning sleep-related aspects like sleep quality or EDS,[10] as well as occurrences of sleep-related hallucinations,[18] have been suggested to potentially correlate with depression. Compared to the former factors, there has been a limited amount of research on the psychosocial factors that impact mental illness in patients with NT1. In our prior study, we proposed a potential association between impulsivity and depressive symptoms.[18] This relationship between depression and impulsivity has also been reported in other studies.[24–26] Therefore, by incorporating impulsivity along with demographic and sleep-related characteristics, it may be possible to predict the presence of depression with appropriate models.

Previous studies have explored the relationship between depression risk factors among patients, which was limited to linear relationships, such as logistic models.[27] However, existing clinical measures for identifying depression are time-consuming and labor-intensive, and often require specialized expertise for result evaluation.[28] Besides, the overlapping symptoms of sleepiness, sleep disturbance, and fatigue,[2,29] between depression and narcolepsy make it challenging to accurately detect and diagnose depression in patients with NT1 using subjective questionnaires. Polysomnography (PSG) and Multiple Sleep Latency Test (MSLT) are validated objective measures for evaluating sleep architecture, quality, and abnormal sleep patterns. Utilizing PSG and MSLT parameters may aid in differentiating depression from narcolepsy. Thus, a novel approach is needed to predict the presence of depression. In contrast to traditional statistical models and diagnostic algorithms, machine learning (ML) has the capability to analyze both linear and nonlinear relationships across high-dimensional data sets,[30,31] making them well-suited for predictive modeling in clinical settings. Recent studies have leveraged ML algorithms to screen or predict diseases, such as obstructive sleep apnea,[32] anxiety and depression.[28,33]

While depression is widely acknowledged as a common comorbidity in NT1, the specific factors that contribute to its development and the effectiveness of predictive models in this context have not been comprehensively explored. This study aims to address this gap by employing machine learning to identify novel predictors and evaluate their potential in improving the early diagnosis and management of depression in NT1 patients.

Methods
Participants
A total of 203 drug-free NT1 patients were recruited at the Sleep Medicine Center of Peking University People's Hospital from September 2019 to April 2023. All patients were consecutively diagnosed with NT1 based on the International

Classification of Sleep Disorders (ICSD-3) criteria: (1) the presence of EDS for at least 3 months; (2) the presence of clear-cut cataplexy, and a mean sleep latency ≤ 8 min with ≥ 2 sleep onset Rapid Eye Movement periods (SOREMPs) during MSLT. REM onset within 15 min of sleep onset during preceding nocturnal PSG may replace one of the SOREMPs during the MSLT. Or without cataplexy but with lower levels of hypocretin (less than 110 pg/mL or one-third of normative values) in CSF. Patients were excluded following the criteria: had a history of mental illness or were having an episode of mental illness. All participants provided written/oral informed consent (for juveniles, the permission of parents/legal guardians also were obtained). This study was approved by the ethics committees of Peking University People's Hospital and conducted by the Declaration of Helsinki.

Input Features

We selected the following potential features based on subjective knowledge and previous studies on risk factors for comorbid depression among patients with NT1. Potential features covering five domains: (1) demographic features: age, gender, body mass index (BMI), education years; (2) clinical features: age at onset, sleep paralysis, hallucinations; (3) self-reported questionnaires: Epworth Sleepiness Scale (ESS), the total and the subscales of Barratt Impulse Scale-11 (BIS-11); (4) PSG parameters: total sleep time (TST), sleep efficiency (SE), nocturnal sleep latency (SL), wake after sleep onset (WASO), R stage (%), N1 stage (%), N2 stage (%), N3 stage (%), apnea-hypopnea index (AHI), arousal index [respiratory-related arousal index (RAI), leg movement-related arousal index (LAI), spontaneous arousal index (SAI)], periodic leg movements index (PLMI); (5) MSLT measurements: The SL in the MSLT.

Measurements

Polysomnography and Multiple Sleep Latency Test

All patients underwent one overnight polysomnography (PSG, Respironics LE-Series Physiological Monitoring System, Alice 6 LE, FL, USA) recording from 10 pm to 6 am. The more detailed information was reported in our previous research.[18] Sleep stages and events were scored by experienced technicians according to the newest American Academy of Sleep Medicine (AASM) manual.[34] The following PSG parameters were collected: total sleep time (TST), sleep efficiency (SE), nocturnal sleep latency (SL), wake after sleep onset (WASO), sleep stages percentages, arousals (respiratory-related arousals index, RAI; leg movement-related arousals index, LAI; spontaneous arousals index, SAI), periodic leg movements index (PLMI), and apnea-hypopnea index (AHI). The MSLT was performed at 2-hour intervals following PSG the night prior. A total of five 20-minute nap opportunities were provided. Each nap was terminated 15 minutes after sleep onset or 20 minutes after wakefulness. Sleep latency was defined as the time from the light off to the first 30-second epoch of any stage of sleep. The mean sleep latency from the 5 naps was calculated.

Demographic and Clinical Characteristics

All patients were systematically evaluated for clinical characteristics including age, gender, body mass index (BMI), age at narcolepsy onset, hypnagogic/hypnopompic hallucination (HH) and sleep paralysis (SP). HH are vivid, dreamlike experiences involving auditory, visual, or tactile sensations that occur either at sleep onset, known as hypnagogic hallucinations, or upon awakening, known as hypnopompic hallucinations.[35] SP is characterized by the temporary inability to speak or move voluntary muscles, typically occurring during transitions between sleeping and waking.[1]

Excessive Daytime Sleepiness

Excessive daytime sleepiness was measured by the Epworth Sleepiness Scale (ESS)[36] or the Epworth Sleepiness Scale for Children and Adolescents (ESS-CHAD).[37] The Chinese version of ESS has been validated in Chinese adults with sleep-disordered breathing showing acceptable internal consistency (Cronbach's α = 0.81).[38] The ESS-CHAD was adapted for children and adolescents aged 7–17 years old,[37] which has been used in our previous study (Cronbach's α = 0.87).[39] The ESS consists of 8 items based on retrospective reports of the likelihood of dozing off or falling asleep in a variety of different situations. Respondents were asked to rate on a 4-point scale (0–3) from would never doze to high chance of dozing. The higher the ESS score indicates the higher their daytime sleepiness.

Depression

The depressive symptoms were assessed by the Center for Epidemiologic Studies Depression Scale for Children (CES-DC)[40] for adolescent NT1 patients or the Self-Rating Depression Scale (SDS)[41] for adult NT1 patients. The Chinese versions of both CES-DC[42] and SDS[43] have been translated and validated within the Chinese population. The CES-DC is a self-administered questionnaire with 20 items. Each item is answered on a 4-point scale (0–3). Total scores range from 0 to 60, with higher scores indicating greater depressive symptomatology. Individuals with a score of 20 or more suggest depressive symptoms.[44] The SDS is also a 20-item scale using a 4-point scale ranging from 1 (none, or a little of the time) to 4 (most, or all of the time). The standardized score of SDS is the raw score multiplied by 1.25, with a cut-off ≥ 53 suggesting depression symptoms.[18] Depression was categorized as a dichotomous variable (depression/non-depression) according to CES-DC or SDS in this study.

Impulsivity Questionnaire

The Barratt Impulse Scale (BIS-11), revised by Patton, Stanford and Barratt, was used to assess impulsive behaviors. The Chinese version of the BIS-11 has been widely used among adolescents[45,46] and adults[47,48] population, showing good internal consistency (Cronbach's α = 0.80–0.92). The BIS consists of three subscales named no-planning impulsivity, motor impulsivity and attentional impulsivity, with each subscale containing 10 items. Each item has 5-point Likert responses from 1 (never) to 5 (always). Individuals with a higher score indicate stronger impulsivity.

Sample Size

The sample size for developing the two-class prediction model was calculated using the "pmsampsize" package in R (version 4.1.1).[49] The calculation was based on a target concordance index of 0.8, considering 5 predictor parameters, and assuming an outcome prevalence of 32%.[7] The analysis indicated that a minimum sample size of 167, with 53 events (events per predictor parameter of at least 10.69), was required for the prediction model development.

Model Building

After partitioning the dataset into a 70:30 split, with 70% allocated for training and 30% for testing, we used 10-fold cross-validation within the training set to build and fine-tune the models. The trained models were subsequently validated on the independent test set to assess their performance. Three classification models were constructed using the Support Vector Machine (SVM), Random forest (RF), and Logistic Regression (LR) algorithms. The LR model, which is a generalized linear regression analysis model, is frequently employed in data mining and disease diagnosis. It was implemented using the "glm" function in the R programming language. The SVM is a supervised learning algorithm particularly effective for high-dimensional data classification. It was implemented using the "e1071" package in R. The optimal parameters for the SVM model are the polynomial kernel with a degree of 2, a scale of 0.01, and C of 0.25. The RF algorithm, which comprises multiple decision trees, was implemented using the R package "randomForest". The 10-fold cross validation was carried out through the R package "caret". Ultimately, the efficacy of the three models was evaluated in the testing sets utilizing receiver operating characteristic (ROC) curves.

Model Evaluation

Model performance metrics included the area under the receiver operating characteristic curve (AUC), accuracy, precision, recall, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and F1 score. The DeLong test was employed to compare the differences between the ROC curves of the various models. Additionally, Decision Curve Analysis (DCA) was conducted for the three models. DCA was developed to evaluate whether the implementation of a prediction model in clinical decision-making would yield more benefits than harms. In summary, a quantitative measure known as net benefit was computed based on the true positive and false positive rates of each model, allowing for a standardized comparison of their advantages and disadvantages.[50]

Statistical Analysis

Descriptive statistics are presented using mean and standard deviation, frequencies, and percentages. Univariate analysis (chi-square test for categorical variables or independent samples t-test for continuous variables) was conducted to compare demographic, clinical characteristics and sleep parameters between depression and non-depression groups. Univariate analyses were conducted using IBM SPSS Statistics 26.0. In contrast, machine learning algorithms were implemented utilizing R software (http://www.R-project.org). Significant differences were found at p-value < 0.05.

Results

Demographics Characteristics of NT1 Patients

Based on the established inclusion and exclusion criteria, a total of 203 NT1 patients (131 males and 72 females), aged 5 to 61 years, were selected for inclusion in this study, comprising 106 adolescents and 97 adults. Among the NT1 patients, 47.8% (97/203) reported experiencing HH, a proportion comparable to those who reported SP (48.8%). The majority (80.8%) experienced narcolepsy onset during childhood or adolescence. The sleep latency in MLST was 1.92 ± 1.79 min. Additionally, EDS symptom was prevalent, as reflected by an ESS score of 17.04 ± 4.62, with a range of 6 to 24. The BIS score was 88.58±15.63, ranging from 41 to 138. Notably, significant differences were observed between the two groups only in the motor impulsivity subscale of the BIS and the presence of HH. Further details are presented in Table 1.

Performance on Different Machine Learning Models and Logistic Regression in the Validation Dataset

Three algorithms, namely LR, RF and SVM, were used to construct a predictive model for depression in NT1 patients. The prediction summary of the models is shown in Table 2. ROC curves and DCA of three models are shown in Figure 1. Additional information from the logistic regression model, such as odds ratio (OR) and confidence interval (CI), was

Table 1 Univariate Analysis Between Depression and Non-Depression Groups (n=203)

Characteristics	Total (n=203)	Non-depression (n=97)	Depression (n=106)	χ^2/T value	P value
Age (at inclusion)	21.10 ± 11.90	21.03 ± 12.94	21.16 ± 10.92	−0.077	0.939
Age group				0.010	0.922
Children and adolescent group	106 (52.2%)	51 (48.1%)	55 (51.9%)		
Adult group	97 (47.8%)	46 (47.4%)	51 (52.6%)		
Gender				0.170	0.680
Male	131 (64.5%)	64 (48.9%)	67 (51.1%)		
Female	72 (35.4%)	33 (45.8%)	39 (54.2%)		
Education years (years)	9.86 ± 4.30	9.27 ± 4.5	10.41 ± 4.06	−1.894	0.060
Hypnagogic/hypnopompic Hallucination				8.476	**0.004**
Yes	97 (47.8%)	36 (37.1%)	61 (62.9%)		
No	106 (52.2%)	61 (57.5%)	45 (42.5%)		
Sleep paralysis				3.142	0.076
Yes	99 (48.8%)	41 (41.4%)	58 (58.6%)		
No	104 (51.2%)	56 (53.8%)	48 (46.2%)		
Age at onset	13.97 ± 10.37	14.32 ± 11.44	13.64 ± 9.32	0.464	0.643
Age onset group				0.711	0.399
Children and adolescent group	164 (80.8%)	76 (46.3%)	88 (53.7%)		
Adult group	39 (19.2%)	21 (53.8%)	18 (46.2%)		
BMI	25.69 ± 5.03	25.26 ± 4.78	26.08 ± 5.24	−1.152	0.251
Polysomnography parameters					
Total sleep time (min)	448.70 ± 69.74	458.45 ± 58.21	439.77 ± 78.04	1.919	0.056
Wake after sleep onset (min)	56.91 ± 47.40	56.9 ± 46.05	56.92 ± 48.82	−0.004	0.997
Sleep efficiency (%)	88.24 ± 9.14	88.48 ± 8.67	88.03 ± 9.58	0.350	0.727
Sleep latency (min)	5.03 ± 8.90	4.69 ± 6.88	5.33 ± 10.43	−0.507	0.613

(*Continued*)

Table 1 (Continued).

Characteristics	Total (n=203)	Non-depression (n=97)	Depression (n=106)	χ^2/T value	P value
Sleep stages					
R (%)	22.11 ± 9.55	21.92 ± 9.09	22.28 ± 9.99	−0.262	0.793
N1 (%)	20.00 ± 13.30	20.96 ± 13.76	19.13 ± 12.87	0.979	0.329
N2 (%)	40.77 ± 11.40	39.85 ± 10.56	41.61 ± 12.09	−1.100	0.272
N3 (%)	16.81 ± 10.08	17.38 ± 10.93	16.28 ± 9.26	0.777	0.438
AHI	6.86 ± 12.04	6.31 ± 9.90	7.37 ± 13.74	−0.625	0.533
Respiratory-related arousals index	3.37 ± 7.62	2.82 ± 5.59	3.88 ± 9.10	−0.994	0.322
Leg movement-related arousals index	1.37 ± 1.88	1.64 ± 2.22	1.13 ± 1.46	1.939	0.054
Spontaneous arousals index	9.99 ± 7.23	10.65 ± 8.23	9.38 ± 6.14	1.251	0.212
PLMI	7.89 ± 12.15	8.89 ± 14.64	6.98 ± 9.29	1.097	0.274
Sleep latency-MSLT (min)[a]	1.92 ± 1.79	1.81 ± 1.67	2.03 ± 1.90	−0.841	0.401
ESS	17.28 ± 5.04	16.89 ± 5.40	17.64 ± 4.67	−1.067	0.287
BIS	76.54 ± 27.03	75.69 ± 28.97	77.31 ± 25.24	−0.426	0.671
Attentional impulsivity score	29.21 ± 7.34	28.90 ± 7.83	29.50 ± 6.89	−0.584	0.560
Motor impulsivity score	28.10 ± 7.30	26.60 ± 7.03	29.48 ± 7.30	−2.861	**0.005**
Non-planning impulsivity score	43.30 ± 25.92	43.14 ± 22.87	43.44 ± 28.54	−0.082	0.935

Notes: [a]Sleep latency refers to the mean sleep latency in the multiple sleep latency test. [b]P value from the Independent sample *t*-test (for continuous data), a Chi-square test or Fisher exact test (for categorical variables). *P* value in bold if < 0.05.
Abbreviations: BMI, body mass index; AHI, apnea hypopnea index; MSLT, multiple sleep latency test; BIS, Barratt Impulse Scale; PLMI, periodic leg movements index; MSLT, multiple sleep latency test; ESS, Epworth Sleepiness Scale.

Table 2 Prediction of Different Machine Learning Models and Logistic Regression in the Validation Dataset (n = 61)

	LR	SVM	RF
AUC (95% CI)	0.543 (0.389–0.697)	0.653 (0.505–0.802)	0.422 (0.27–0.575)
Accuracy (95% CI)	0.537 (0.374–0.693)	0.659 (0.494–0.799)	0.415 (0.263–0.579)
Balanced Accuracy	0.543	0.653	0.422
Sensitivity	0.455	0.727	0.318
Specificity	0.632	0.579	0.526
Positive predictive value	0.588	0.667	0.438
Negative predictive value	0.5	0.647	0.4
Prevalence	0.537	0.537	0.537
Precision	0.588	0.667	0.438
Recall	0.455	0.727	0.318
F1 Score	0.513	0.696	0.368
Kappa	0.085	0.308	−0.152

Abbreviations: AUC, area under receiver operating characteristic curve; CI, confidence interval; LR, logistic regression; SVM, support vector machine; RF, random forest.

shown in Supplementary Table 1. Using the clinical and sleep metrics as features of the SVM classification model achieved better performance in distinguishing depression from non-depression. Briefly, the SVM model classification of accuracy was 0.659, specificity was 0.579, sensitivity was 0.727, PPV was 0.667, and NPV was 0.647 in the test set. The DCA of the SVM model classification was also better than other models (Figure 1b). The SVM classification importance of each feature was further examined, and the results are presented in Figure 2.

Discussion

Depression is a prevalent comorbidity among patients with NT1. Despite many studies investigating the relationship between narcolepsy and depression, a robust predictive model for depression in NT1 patients remains elusive. This study
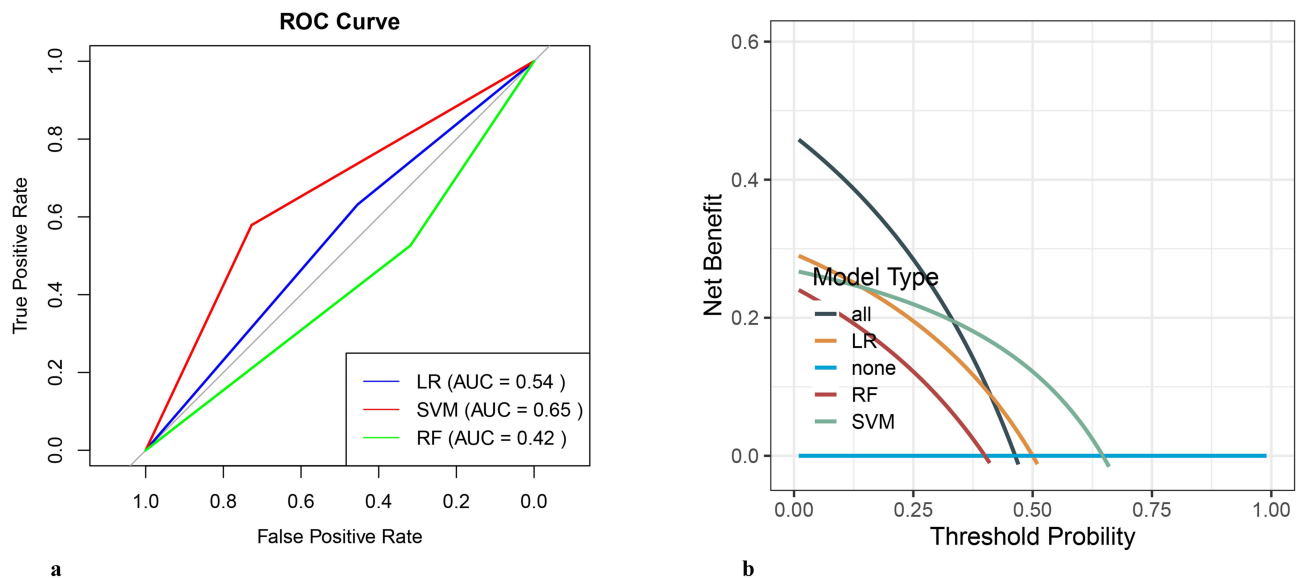
Figure 1 (**a**) The receiver operating characteristic curve of the models. (**b**) The decision curve analysis of the models.
Abbreviations: ROC, receiver operating characteristic curve; LR, logistic regression; RF, random forest; SVM, support vector machine.
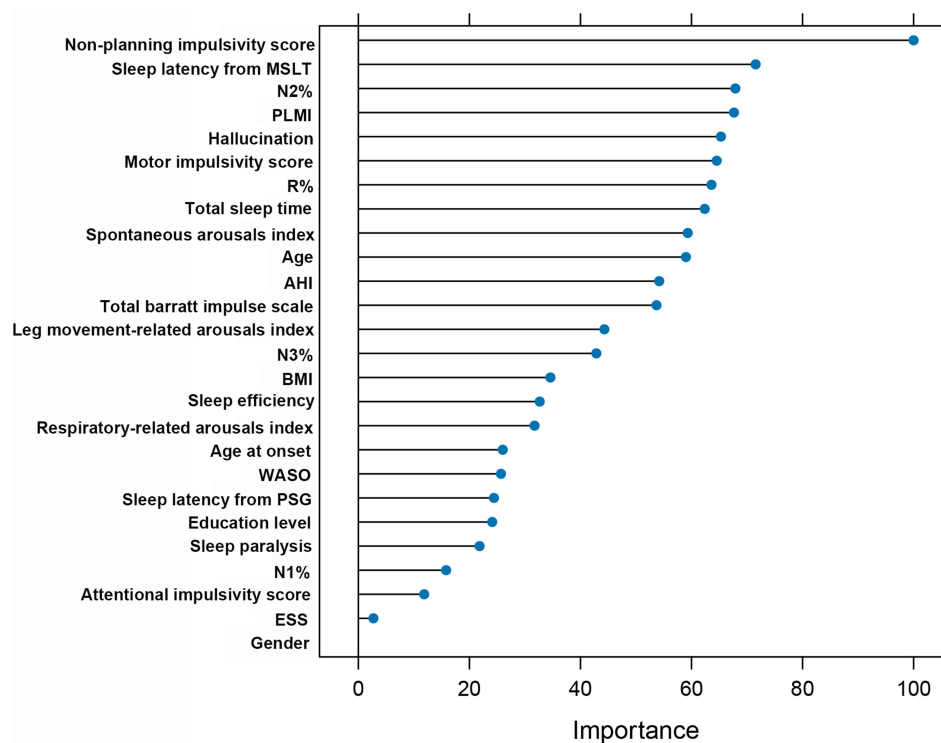

Figure 2 The importance index of all variables from the support vector machine model.
Abbreviations: BMI, body mass index; ESS, Epworth Sleepiness Scale; WASO, wake after sleep onset; PLMI, periodic leg movements index; AHI, apnea-hypopnea index.

presents evidence supporting the efficacy of ML tools in predicting depression among patients with NT1. The LR model identified hallucinations and motor impulsivity as predictors of depression. Additionally, our SVM model incorporating routinely collected clinic variables, PSG parameters, ESS scores, and BIS scores outperformed the traditional LR model in predicting depression. Consequently, using readily available data from the PSG parameters, ML algorithms offer a more efficient approach for large-scale identification of depression among patients with NT1.

In this study, 52.2% of NT1 patients (52.6% of adults and 51.9% of children and adolescents) reported experiencing depression symptoms, a rate higher than that reported in a systematic review (32%, 95% CI, 28–36%).[7] This discrepancy may be due to the measurement tool we used, which could overestimate depression prevalence compared to studies employing the Diagnostic and Statistical Manual of Mental Disorders (DSM-III/IV) criteria or psychiatric interviews. The prevailing consensus in the literature is that the high prevalence of depression/depressive symptoms among narcolepsy patients is primarily attributed to hypocretin deficiency[51–53] and its subsequent effects caused by narcolepsy disease, such as poor quality of life or social stigma.[7,27]

Motor impulsivity was also associated with depressive symptoms in children and adolescents with NT1, a relationship that we previously identified.[18] This relationship may be rooted in the pathophysiology of NT1, particularly hypocretin deficiency, which is associated with emotion regulation and stress-adaptive responses.[15] The lack of hypocretin may impair emotional responses, leading to increased impulsivity and a higher risk of depression. In addition, a study examining brain structure in children and adolescents has demonstrated that both depression and impulsivity are associated with cortical thickness. Similarly, our findings indicate that the depressive symptoms and impulsivity in NT1 patients are linked to morphological changes in the cerebral cortex[54] and alterations in default mode network connectivity.[55]

The HH symptom was found to be independently associated with depressive symptoms among patients with NT1, consistent with findings from previous studies.[8,27] The association between HH and depression is noteworthy and may be attributed to several overlapping physiological and psychological mechanisms. Firstly, narcolepsy is characterized by abnormal regulation of REM sleep, which is closely linked to the occurrence of hallucinations.[56] The REM sleep dysregulation has also been implicated with mood disorders, particularly depression.[57] Furthermore, hypocretin deficiency, the hallmark of NT1, is thought to contribute to both hallucinations and depressive symptoms.[52] Finally, the distress caused by hallucinations, which can be disturbing and frightening, may exacerbate or contribute to the progression of depressive symptoms in NT1 patients.[58]

Our research primarily focuses on children and adolescents, who constitute 80% of patients presenting symptoms, a demographic distinct from adults in terms of depression-related factors. Additionally, our patient cohort exhibits a higher prevalence of sleep-related symptoms, such as hallucinations, compared to other studies. We have also included impulsivity as a potential non-sleep symptom factor in our analysis. Given these considerations, age-specific symptom development, the prevalence of sleep-related symptoms, and the role of impulsivity, our results may differ from those of previous research.

ML has been extensively applied in mental health for detection, diagnosis, prognosis, and treatment, particularly in depression, schizophrenia, and Alzheimer's Disease.[59] However, research on utilizing these algorithms to predict depression in patients with NT1 remains limited. Our study demonstrates that the SVM model, incorporating both clinical factors and PSG parameters, exhibited superior performance relative to other machine learning models tested (Table 2), as evidenced by its higher net benefit in decision curve analysis, in NT1 patients. Consistent with previous studies,[60–62] the SVM algorithm demonstrated the optimal performance in developing ML models for depression prediction. When identifying depression in NT1 patients, it is crucial to comprehensively and precisely identify emotional difficulties. The SVM model performs better with an AUC of 0.653, showing good discriminative ability. The accuracy of 0.659 and balanced accuracy of 0.653 are strong, suggesting that the model is effective at classifying both positive and negative cases. It also exhibits high sensitivity (0.727) and recall (0.727), indicating its strength in detecting positive cases. However, the specificity (0.579) is lower compared to LR, and the F1 Score (0.696) and Kappa (0.308) suggest a generally better performance but with room for improvement. The models were trained on a subset of the available data and tested independently. However, to truly measure generalizability, it is necessary to test the models on external datasets or in real-world scenarios. Limited external validation may affect the robustness and applicability of our findings across diverse populations or settings. Although we employed 10-fold cross-validation to mitigate overfitting by validating the model on different subsets of the training data, this technique cannot eliminate the risk.

The ML model can be integrated into clinical practice to enhance early detection of depression in NT1 patients, enabling timely and personalized interventions. By serving as a decision-support tool, it can help clinicians prioritize at-risk patients for further evaluation and targeted care. Additionally, the model's adaptability allows for continuous

improvement as new biomarkers and psychological variables are incorporated, ensuring it remains a valuable resource in managing NT1 and its comorbidities.

Limitations

This study has several limitations. Firstly, this study is based on cross-sectional data, which prevents the establishment of a causal relationship between the factors investigated in our research and depression outcomes. Secondly, the sample size was relatively small; however, it should be noted that even smaller sample sizes have been used in other published studies employing SVM for clinical medicine, eg, 71 participants[60] and 55 participants.[61] The ML algorithm may achieve more optimal performance with larger input data;[49] therefore, further validation of these models using additional data is warranted. Thirdly, the depressive symptoms were assessed by a scale, which is not the gold standard for the diagnosis of depression, although the scales have been extensively used and validated in previous studies.[18,23,33] Lastly, the absence of psychological factors data among patients with NT1 poses a limitation in exploring potential causes for depression within this study. Given the multifaceted nature of depression, future research should consider integrating additional psychological variables, such as stigma, resilience, and coping strategies, into the model to improve its sensitivity and predictive accuracy. Beyond psychological factors, exploring potential biomarkers, such as inflammatory markers or neuroimaging data, and incorporating novel data sources like real-time digital health metrics or genetic information could further enhance the model's predictive power.

Conclusion

This exploratory study demonstrates the potential of ML models in addressing clinical challenges related to depression in NT1 patients. Our findings indicate that depression in NT1 is significantly associated with sleep-related hallucinations and impulsivity. The models developed herein provide promising tools for identifying NT1 patients at elevated risk for depression, paving the way for the development of a data-driven, personalized decision-making framework. Such a tool could significantly enhance the efficiency of depression diagnoses in NT1 patients. Future research should focus on validating these findings across diverse populations and incorporating additional psychological variables to further refine and improve the model's precision.

Disclosure

The authors have no conflict of interest to declare.

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