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ORIGINAL ARTICLE

Characterising the motion and cardiorespiratory interaction of preterm infants can improve the classification of their sleep state

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Abstract

Aim: This study aimed to classify quiet sleep, active sleep and wake states in preterm infants by analysing cardiorespiratory signals obtained from routine patient monitors.

Methods: We studied eight preterm infants, with an average postmenstrual age of 32.3 ± 2.4 weeks, in a neonatal intensive care unit in the Netherlands. Electrocardiography and chest impedance respiratory signals were recorded. After filtering and R-peak detection, cardiorespiratory features and motion and cardiorespiratory interaction features were extracted, based on previous research. An extremely randomised trees algorithm was used for classification and performance was evaluated using leave-one-patient-out cross-validation and Cohen's kappa coefficient.

Results: A sleep expert annotated 4731 30-second epochs (39.4 h) and active sleep, quiet sleep and wake accounted for 73.3%, 12.6% and 14.1% respectively. Using all features, and the extremely randomised trees algorithm, the binary discrimination between active and quiet sleep was better than between other states. Incorporating motion and cardiorespiratory interaction features improved the classification of all sleep states (kappa 0.38 ± 0.09) than analyses without these features (kappa 0.31 ± 0.11).

Conclusion: Cardiorespiratory interactions contributed to detecting quiet sleep and motion features contributed to detecting wake states. This combination improved the automated classifications of sleep states.

KEYWORDS
automated classification, cardiorespiratory signal, motion, preterm infant, sleep

Abbreviations: AUC, area under the curve; CRI, cardiorespiratory interaction; ECG, electrocardiography; REM, rapid eye movement.

1 | INTRODUCTION

Sleep is one of the most important factors in the neural development of preterm infants. This implies that continuous sleep monitoring may provide an indicator of neural development over time.[1,2] Previous research has shown that sleep impacts the physiology of preterm infants. For example, heart rate variability and respiratory activity have been reported to change during sleep.[3,4] Adult sleep is classified into three states: rapid eye movement (REM), non-rapid eye movement and wake, based on manual scoring from polysomnography.[5] The non-rapid eye movement is further divided into three sleep states: N1, N2 and N3. Sleep scoring in preterm infants is often based on behavioural observation. This is because their brain is at a premature developmental stage, where identifying rapid eye movement and non-rapid eye movement with absolute clarity is challenging. Hence, the sleep classifications of preterm infants are limited to active sleep, quiet sleep and wake.[6]

Sleep states in infants have been associated with specific states of development. Hence, the distribution of sleep states can serve as an indicator of brain maturation in preterm infants.[7] Active sleep is necessary for the early development of the sensory and hippocampal systems required for memory creation.[8] Quiet sleep is important for the pre-consolidation of learning and memory development from sensory experiences, including vision, hearing and touch. In addition, quiet sleep impacts brain size and plasticity in infants as they transition to adulthood.[9] Over time, preterm infant sleep state patterns change, with a reduction in active sleep and a concomitant increase in quiet sleep and wake.[9]

The annotation of various sleep states is aided by a variety of physiological measures, such as electroencephalography, electromyography, electrocardiography (ECG), respiration and oxygen saturation.[5] The process of sleep scoring, based on polysomnography, involves an expert scorer who visually analyses a series of 30-second epochs of multichannel signals and assigns each epoch to a specific stage of sleep. However, these methods are time-consuming and costly. More importantly, many signals, such as electroencephalography, amplitude-integrated electroencephalography and electromyography, are not routinely measured in the neonatal intensive care unit. Adding electrodes to measure these signals would significantly increase the risk of skin damage in preterm infants.[1] Another validated approach for scoring sleep states in preterm infants is behavioural observation.[10] Otte et al. analysed agreements between the behavioural and polysomnography sleep scoring approaches in infants under 1 year of age. The authors found strong agreement, with a Cohen's kappa value of ≥0.74, particularly when they compared wake, active sleep and quiet sleep annotation with wake: REM/N1/N2, and N3 sleep (kappa = 0.85).[10] However, behavioural sleep scoring involves manual annotation that requires considerable effort. Therefore, it is imperative to analyse preterm infant sleep patterns by employing existing sensors already installed in the neonatal intensive care unit. These include ECG and chest impedance respiratory signals.

Key notes

- This study aimed to verify the feasibility of automated classifications of sleep states of preterm infants, using cardiorespiratory signals from routine patient monitoring.
- A sleep expert annotated 4731 30-second epochs (39.4 h) and reported that active sleep, quiet sleep and wake accounted for 73.3%, 12.6% and 14.1% respectively.
- We found that using features extracted from motion and cardiorespiratory interaction improved the sleep state classification performance.

Machine learning techniques that are based on cardiorespiratory parameters have been employed to classify infant sleep.[11] For example, Harper et al. used cardiorespiratory signals to determine the sleep states of full-term infants and achieved an accuracy of 80%.[12] Werth et al. initially achieved a kappa score of 0.30 in classifying sleep states in eight preterm infants using features extracted from ECGs and a random forest classifier.[9] Subsequently, the same authors slightly improved the kappa score to 0.33 by implementing a convolutional neural network.[13] Sentner et al. reported a kappa score of 0.24 when detecting sleep states using heart rate, respiratory rate and oxygen saturation that was directly obtained from the patient monitor.[14] Nevertheless, the existing sleep scoring models have relatively low performance and are not ready for use in clinical practice.

Extracting more informative features from cardiorespiratory signals may provide additional information to improve sleep state classifications in preterm infants. In this study, we considered the information related to body movements and cardiorespiratory interactions. Cardiorespiratory interaction (CRI) is the interaction between cardiac and respiratory dynamics.[15] For each 30-second epoch, this interaction is constructed by identifying the heartbeats and determining the amplitude of respiratory signal at the corresponding time stamp. Our previous studies demonstrated an association between cardiorespiratory interaction and preterm infant sleep state using the visibility graph method.[16] In addition, an infant's body movement is highly correlated with sleep and wake states and can be well estimated by quantifying the motion artefacts modulated in ECG and respiratory signals.[16,17] Peng et al. proposed a method that combined continuous wavelet transform and signal instability indexing to quantify body motion in preterm infants using ECGs or respiratory signals.[18] They obtained an area under the receiver operating characteristics value of 0.92. In this study, we proposed extracting motion signal features obtained via the motion detection method and from the cardiorespiratory interaction signals derived from the visibility graph complex network analysis.[15]

The aim of this study was to improve the sleep classification accuracy in preterm infants by incorporating these novel features along with the ECG features proposed by Werth et al.[19] and the respiratory features commonly used in adult sleep staging.[20]

2 | METHODS

2.1 | Data and sleep annotation

Chest impedance respiratory and ECG data that were routinely collected from the patient monitors of eight clinically stable preterm infants were analysed. These infants were admitted to the neonatal intensive care unit of the Máxima Medical Centre, Veldhoven, the Netherlands, in 2012. The mean and standard deviation age of the selected infants was 30.0 ± 2.3 weeks of gestation and the birth weight was 1680.8 ± 634.3 grams. Their mean postmenstrual age during the study was 32.3 ± 2.4 weeks. None of the infants exhibited signs or symptoms of neonatal seizures. The Ethical Committee of the Máxima Medical Center approved the study and the parents of the preterm infants provided written, informed consent.

We employed the behavioural sleep annotation system developed for infants by Otte et al.[10] A trained sleep expert annotated sleep states in 30-second, non-overlapping windows, based on videos of the sleeping infants and respiratory signals. The sleep states were originally annotated into five categories: quiet sleep, active sleep, wake, caretaking and unknown.[19] Caretaking epochs were defined as the periods when the preterm infants received routine care from nurses or neonatologists in the neonatal intensive care unit. Unknown epochs were those that could not be annotated, for example, if the infants were not in the incubator or were not visible in the video. A total of 4815 epochs (40.1 h) were annotated and active sleep, quiet sleep, wake, caretaking and unknown accounted for 72.0%, 12.4%, 2.5%, 11.4% and 1.7% respectively. Since preterm infants are mostly awake during the caretaking stage, we merged caretaking and wake into one state and called this wake. Unknown epochs were excluded from the analysis. This meant that 4731 epochs (39.4 h) of data for the eight preterm infants were used in this study, with an average recording time of 591 ± 175 epochs (4.9 ± 1.5 h). Table 1 shows the distribution of the sleep states in this study.

2.2 | Signal preprocessing

ECG data were recorded at 500 Hz and respiratory data at 16 Hz, using chest impedance electrodes from a Philips Monitor Intellivue Mx800 (Philips Medical Systems, Baden-Württemberg, Germany). To remove noise from the respiratory signals, a 10th-order Butterworth bandpass filter (0.005–2 Hz), implemented in Matlab (MathWorks, Massachusetts, USA), was used. Subsequently, we subtracted the baseline from the respiratory signal obtained using a median filter with a 1-second window. For ECG signals, a type-II Chebyshev filter (0.001–120 Hz), implemented in Matlab, was applied to remove baseline wander. To extract features related to heart rate variability, the R-peaks of ECG data were detected using an existing QRS detection algorithm (Ralph Wijshoff et al., Noord Brabant, The Netherlands).[21]

As previously stated, the presence of motion artefacts is considered an indicator of certain sleep states, such as wake. This study extracted motion signals from both ECG and respiratory signals using the combined continuous wavelet transform and signal instability indexing algorithm. Our previous study investigated cardiorespiratory interactions in preterm infants using the visibility graph method. This method involves constructing a cardiorespiratory interaction signal by utilising the timing of the R-peak in each heartbeat from the ECG signal and the amplitude of the respiratory signal at the corresponding timestamp. Figure 1 illustrates the signal pre-processing of raw ECG and chest impedance respiratory signals collected from patient monitors. This yielded four signals that were used for feature extraction.

2.3 | Features

Based on previous studies, 34 cardiac features were extracted from filtered ECG signals[19] and 41 from filtered chest impedance respiratory signals.[20] As preterm infants have a higher heart rate and breathing rate than adults, adaptations were made to accommodate such differences in some features. Detailed explanations of the cardiac and respiratory features are provided in Tables S1 and S2 respectively. In addition, we extracted 20 new features from the motion and cardiorespiratory interaction characteristics, to improve cardiorespiratory-based sleep state classification in preterm infants.

From the two motion signals, one derived from the ECG signal and one other from the respiratory signal, we extracted 12 motion features for each epoch. The sum of all motion values of each epoch was computed, where a larger sum corresponded to a stronger movement. The standard deviation of motion quantified the variation in body movement. We also computed the 50th, 75th, 90th

TABLE 1 The distribution of annotated sleep states.

Sleep state (30-second epoch)	Subject								
	1	2	3	4	5	6	7	8	Mean ± SD
Quiet sleep	145	134	18	111	74	59	24	30	74.4 ± 50.4
Active sleep	455	392	550	491	431	676	211	259	433.1 ± 150.2
Wake	134	75	35	29	164	63	4	167	83.9 ± 63.4
Total epochs	734	601	603	631	669	798	239	456	591.4 ± 174.6

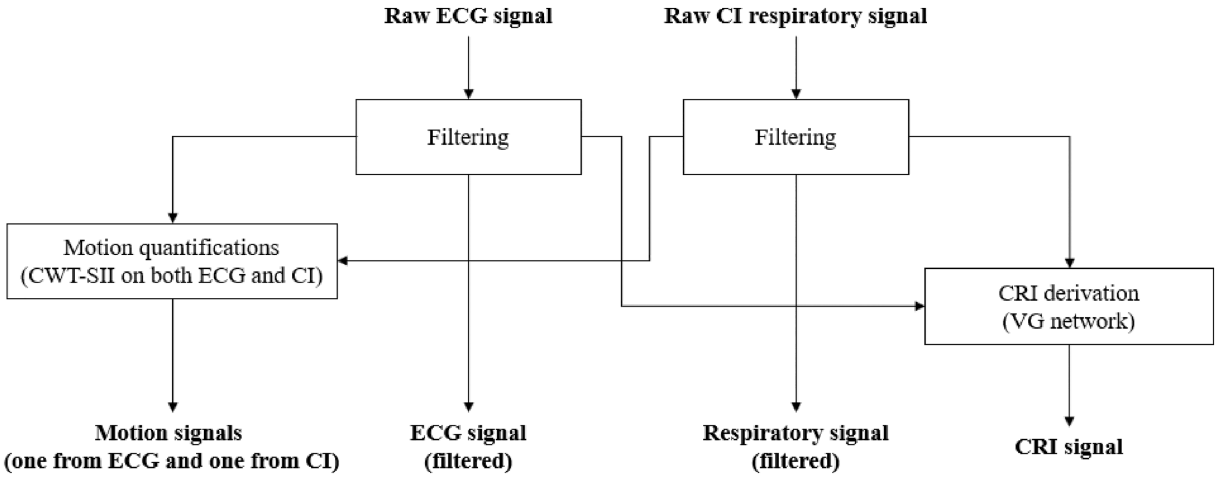

FIGURE 1 Schematic diagram of the preprocessing of raw ECG and chest impedance respiratory signals. CI, chest impedance; CWT-SII, continuous wavelet transform-signal instability index; ECG, electrocardiography; VG, visibility graph.

and 95th percentiles of the motion values. Table S3 summarises the motion features proposed by this study.

Several parameters of the visibility graph network topology constructed from the cardiorespiratory interaction time series exhibited significant differences among the preterm infant sleep states.[15] Therefore, we extracted eight features from the cardiorespiratory interaction signals. The means and standard deviations of the degree of the cardiorespiratory interaction network were constructed using the visibility graph method and the network created with the difference visibility graph[22] was calculated. The assortative coefficient is a measure of assortative mixing by degree and it represents the skewness in the connections of network nodes.[15] The clustering coefficient quantified the density of the local clusters within a network. The means and standard deviations of the clustering coefficient values were calculated for each epoch. The sample entropy of the network degrees was computed to quantify the regularity of the cardiorespiratory interaction networks. We also extracted features from the degree distribution to examine the statistical properties of the cardiorespiratory interaction network.[15] An overview of the cardiorespiratory interaction network features is provided in Table S4.

To reduce the high-frequency noise conveyed by features that did not reflect changes in the sleep state, the features were smoothed using a low-pass filter. For the smoothing window size, an experimental choice of 19 epochs (9.5 min) was used. This choice was made because most periods of a certain sleep state in our dataset lasted for more than 10 min.

2.4 | Classification algorithms

Sentner et al.[14] have previously demonstrated the successful application of tree-based machine learning algorithms, such as random forest, in the classification of cardiorespiratory sleep states in preterm infants. The extremely randomised trees classifier is another tree-based algorithm that uses the entire original sample, in contrast to the bootstrapping approach employed by random forests. Random cut points were selected to split the nodes during the tree construction. Moreover, compared to random forests, extremely randomised trees are considered to have less bias and computational costs.[23] Hence, we employed both random forest and extremely randomised trees for comparison when classifying preterm infant sleep states. The tree-based classifier parameters were selected empirically. The maximum depth, minimum number of samples required to split an internal node, minimum number of samples needed to be in a leaf node and number of trees in the forest were set to 10, 10, 4 and 300 respectively.

As previously mentioned, the distribution of sleep states was highly imbalanced, with active sleep accounting for the majority (>70%) of the total epochs. In such cases, machine learning models can be heavily biased towards the majority class. This may result in a poor performance in the minority class. To resolve this issue, we followed Werth et al.'s approach[19] and employed a synthetic minority oversampling technique during model training, to increase the number of quiet sleep and wake samples. Notably, the synthetic minority oversampling technique was not applied to the test data.

2.5 | Validation and evaluation

Leave-one-patient-out cross-validation was used to train and test the proposed method for classifying the sleep states of preterm infants. The full dataset was randomly split into eight folds by each infant, where the number of folds was equal to the number of infants. During each round of the leave-one-patient-out cross-validation, seven infants were used to train the model and the remaining one was used to test the trained model. The sleep classification results of all the infants are reported as means and standard deviations.

Extensively used metrics were considered first to evaluate the models for classifying preterm infant sleep states, including the overall accuracy, sensitivity, precision and confusion matrix.

However, owing to the presence of an imbalanced distribution of classes, the use of overall accuracy can be misleading and model training and optimisation can be strongly biased towards the majority class.[24] Cohen's kappa coefficient value, independent of chance agreement, has been widely accepted in assessing infant sleep classification performance. According to Landis and Koch, a kappa value of <0 is considered as no agreement, 0–0.20 as slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial and 0.81–1 as almost perfect agreement.[25] In addition, we plotted the receiver operating characteristics curves and reported the area under the curve (AUC) and kappa values to distinguish between each of the two sleep states. These were: active sleep versus quiet sleep, quiet sleep versus wake, active sleep versus wake and wake versus sleep including active sleep and quiet sleep. The classification between the two states was retrained and tested using extremely randomised trees and all features were subjected to the same leave-one-patient-out cross-validation procedure. To confirm the added value contributed by the new motion and cardiorespiratory interaction features in sleep state classification, we compared the performance using all features with three other feature sets. These were one feature set that comprised ECG and respiratory features, one with ECG, respiratory and motion features and one with ECG, respiratory and CRI features. The model parameters were optimised for the training data during each round of leave-one-patient-out cross-validation to maximise the kappa coefficient value.

3 | RESULTS

Table 2 presents the sleep state classification performance by accuracy and Cohen's kappa coefficient, using all features. The results include leave-one-patient-out cross-validation performance for each infant and means and standard deviations for all infants. Extremely randomised trees achieved a kappa of 0.38 ± 0.09, which was better than the random forest approach (0.31 ± 0.14). However, this difference was not statistically significant examined using the Mann–Whitney *U* test ($p = 0.29$). Both methods outperformed the results obtained in previous work that just used ECGs.[19]

We also compared the performances of sleep classifications based on extremely randomised trees, using different feature sets (Table 3). Interestingly, combining all the features achieved the best performance, with reduced variability compared to the other feature sets. Notably, both cardiorespiratory interactions and motion features independently contributed to performance improvement. The confusion matrices, which were obtained using different feature sets, are shown in Figure 2. This analysis demonstrated a notable improvement in the detection of wake using motion features during sleep. In addition, cardiorespiratory interaction features were helpful in distinguishing quiet sleep from the other two sleep states.

To understand the importance of features in classifying sleep states, Figure 3 lists the top 10 features, ranked by their Gini importance scores in extremely randomised trees when we used all the features. These included the five respiratory features, four motion features and one cardiorespiratory interaction feature. In addition to the respiration signal containing important features, several motion features were highly ranked, indicating their important contribution to boosting the classification. This was because of their ability to detect wake and caretaking states from sleep states.

The receiver operating characteristics curves for classifying each of the two sleep states are shown in Figure 4 to demonstrate how well the algorithm could separate different sleep states. The discrimination between active sleep and quiet sleep (AUC 0.93 ± 0.05, kappa 0.56 ± 0.12) was clearly better than that between other states, in particular, the discrimination between active sleep and wake (AUC 0.68 ± 0.12, kappa 0.19 ± 0.14), which was difficult to distinguish.

4 | DISCUSSION

This study demonstrated that preterm infant sleep state classification results improved when they were based on cardiorespiratory signals. This was because we used additional features, extracted from the signals, which characterised body movements and the interaction between cardiac and respiratory activities. In addition, the extremely randomised trees classifier outperformed the widely

TABLE 2 Performance of preterm infant sleep state classification (active sleep, quiet sleep and wake) using random forest and extremely randomised trees based on all features.

	Random forest		Extremely randomised trees	
Subject	Accuracy	Kappa	Accuracy	Kappa
1	0.72	0.40	0.76	0.49
2	0.72	0.43	0.72	0.43
3	0.92	0.33	0.89	0.47
4	0.56	0.31	0.69	0.41
5	0.72	0.50	0.67	0.42
6	0.68	0.15	0.79	0.32
7	0.53	0.16	0.67	0.30
8	0.58	0.17	0.52	0.19
Mean ± SD	0.68 ± 0.13	0.31 ± 0.14	0.71 ± 0.11	0.38 ± 0.09

TABLE 3 Performance comparison using different feature sets in classifying preterm infant sleep states (active sleep, quiet sleep and wake) using extremely randomised trees.

	Feature set			
Performance metric	ECG and respiratory	ECG, respiratory and CRI	ECG, respiratory and motion	ECG, respiratory, motion and CRI
Accuracy	0.70 ± 0.13	0.69 ± 0.16	0.70 ± 0.10	**0.71 ± 0.11**
Kappa	0.31 ± 0.11	0.33 ± 0.13	0.36 ± 0.09	**0.38 ± 0.09**
Sensitivity active sleep	**0.78 ± 0.20**	0.76 ± 0.18	0.76 ± 0.14	**0.78 ± 0.13**
Precision active sleep	0.84 ± 0.12	0.84 ± 0.11	**0.85 ± 0.11**	**0.85 ± 0.11**
Sensitivity quiet sleep	0.69 ± 0.29	0.74 ± 0.22	**0.80 ± 0.21**	**0.80 ± 0.18**
Precision quiet sleep	**0.54 ± 0.16**	0.53 ± 0.18	0.48 ± 0.17	0.51 ± 0.18
Sensitivity wake	0.33 ± 0.35	0.28 ± 0.24	0.34 ± 0.22	**0.36 ± 0.22**
Precision wake	0.39 ± 0. 41	**0.52 ± 0.36**	0.44 ± 0.28	0.39 ± 0.33

Note: Results are presented in mean ± SD. The best result of each performance metric is indicated in bold.

Abbreviations: CRI, cardiorespiratory interaction; ECG, electrocardiography.

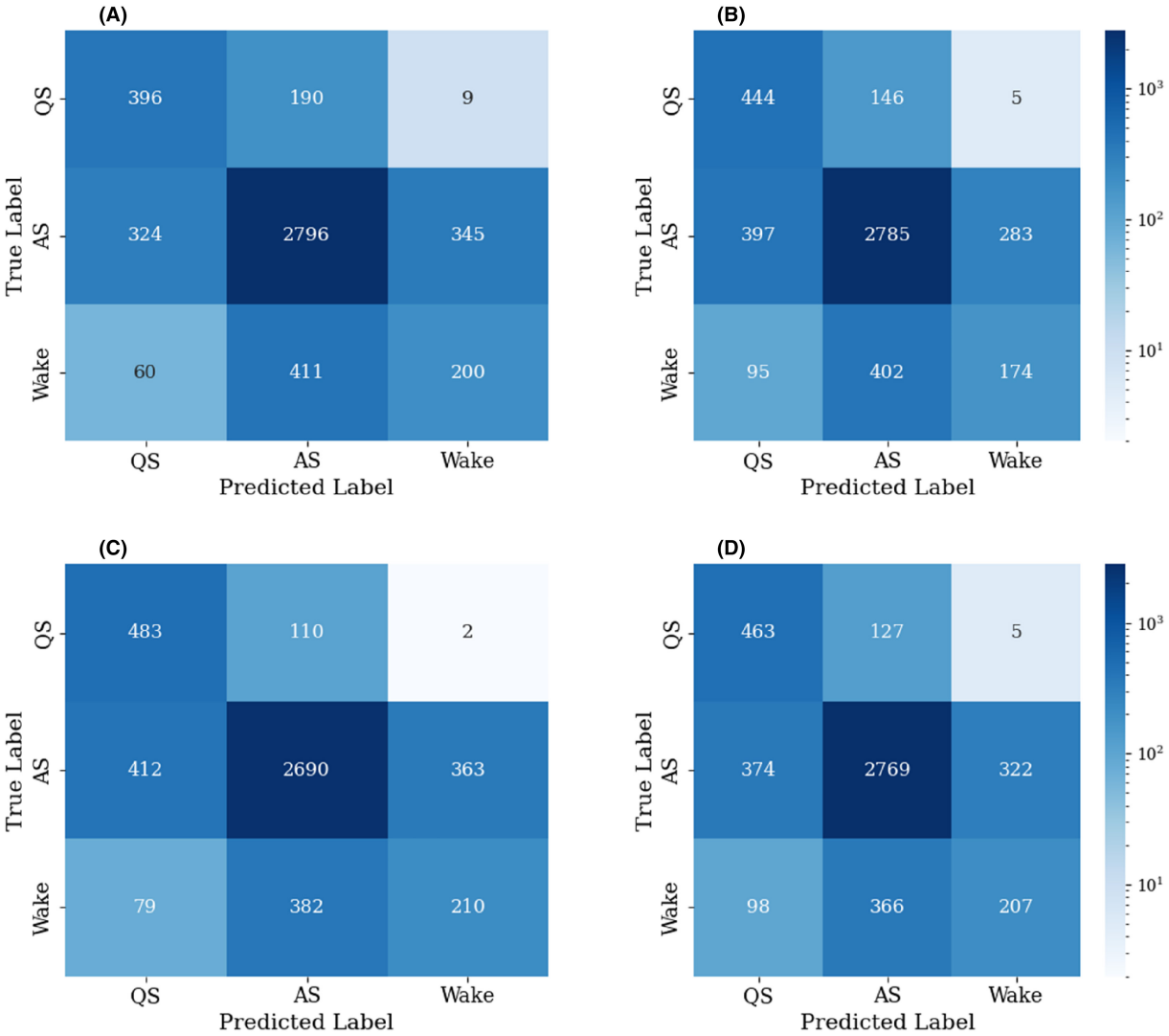

FIGURE 2 Confusion matrices in preterm infant sleep state classification (active sleep, quiet sleep and wake) using feature set (A) ECG and respiratory features, (B) ECG, respiratory and cardiorespiratory interaction features, (C) ECG, respiratory and motion features, (D) ECG, respiratory, motion and cardiorespiratory interaction, where aggregated results of all epochs were presented. AS, active sleep; ECG, electrocardiography; QS, quiet sleep.

used random forest classification algorithm, although the difference was not statistically significant.

As shown in Figure 3, five new features were in the list of the top 10 features, which comprised one cardiorespiratory interaction feature, five respiratory features and four motion features. The top three important features were respiratory features, consistent with the behavioural sleep annotation approach that relies heavily on breathing information.[10] Nonetheless, ECG features should also be considered vital contributors to the classification and the most important ECG features made the list of the top 20 features. Heart rate variability during sleep, particularly quiet sleep, exhibited greater stability in preterm infants than during active sleep and wake.[26]

Motion features were also highly ranked in terms of their importance. The presence of motion artefacts has been recognised as an indicator of wake and/or caretaking, as previously reported. Including motion features in the classification scheme can significantly improve the classification performance (Figure 2 and Table 3), contributing to distinguishing between quiet sleep and active sleep or wake with the presence of increased body movements.[10] Interestingly, the top-ranked motion features were all extracted from motion signals derived from ECGs instead of respiration from the chest impedance. One possible reason for this is that body movements detected by ECG are more sensitive than respiration.[27] Peng et al.[18] studied a similar population. They reported that using the combined continuous wavelet transform and signal instability indexing algorithm demonstrated that electrocardiography-based motion detection had superior performance to respiration-based detection, especially in detecting gross motor motion. The best cardiorespiratory interaction feature was sample entropy of degree, which is defined as the sample entropy of the node degree of the constructed cardiorespiratory interaction network. It measures the regularity or stability of cardiorespiratory interaction patterns. A higher sample entropy of degree value corresponds to a lower regularity in the cardiorespiratory interaction time series, which is more likely to be associated with wake and caretaking states.[28] This indicates its ability to distinguish the sleep states of preterm infants. For example, Figure 2 shows that including cardiorespiratory interaction features generally led to fewer false detections of active sleep, which might likely be less irregular in the cardiorespiratory interaction pattern compared to wake, but is more irregular than quiet sleep.

Combining the new features proposed in this study with existing ECG and respiration features resulted in an overall improvement in classifying preterm infant sleep states. The mean kappa value increased from 0.31 ± 0.11 to 0.38 ± 0.09, approaching moderate agreement between the automated sleep state classification and human annotation and outperforming previously results reported.[18] We also confirmed the advantages of using the extremely randomised trees classifier instead of the random forest algorithm (Table 2). However, a relatively large variation in the classification performance between subjects can be seen in that table. One explanation could be the marked difference in sleep state distribution, where, for example, subject seven had only four wake epochs, which was much fewer than the other subjects. During such a short wake period, changes in the cardiorespiratory activity regulated by the autonomic system were apparently not sufficient. Inspecting the video recording showed found that the

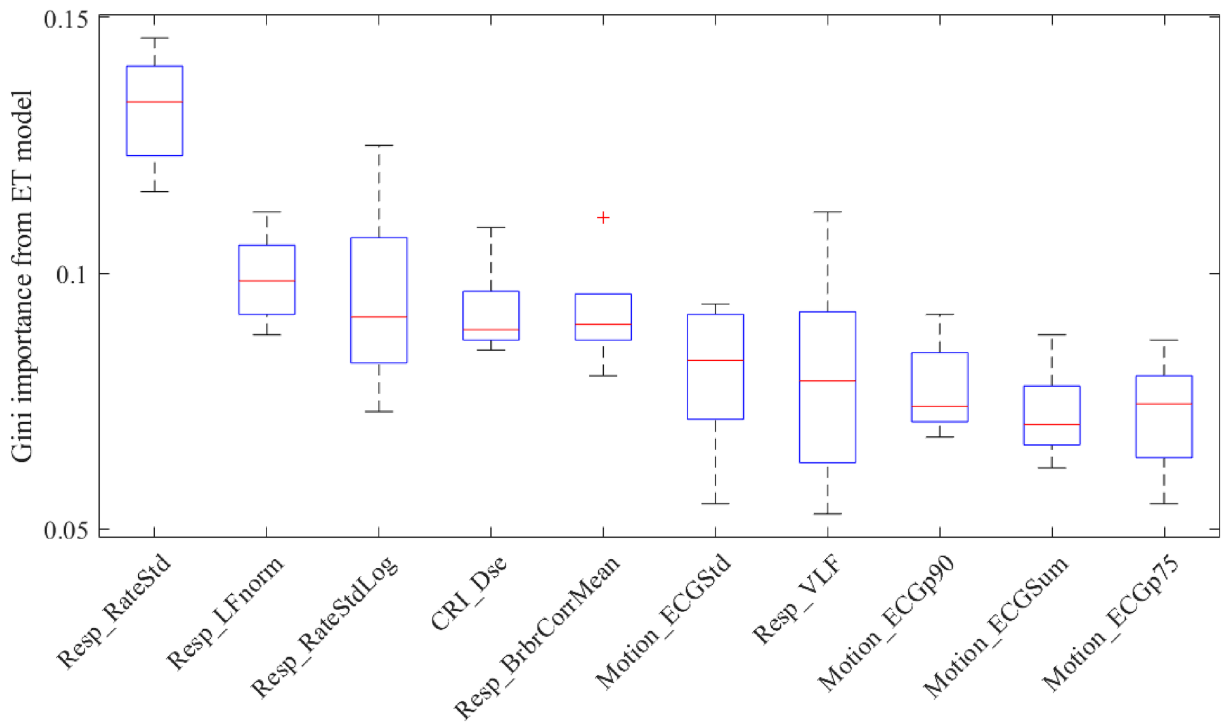

FIGURE 3 Box plots of the top 10 features in sleep state classification based on extremely randomised trees Gini importance (across subjects). Feature names and their description can be found in the Tables S1–S4. ET, extremely randomised trees.

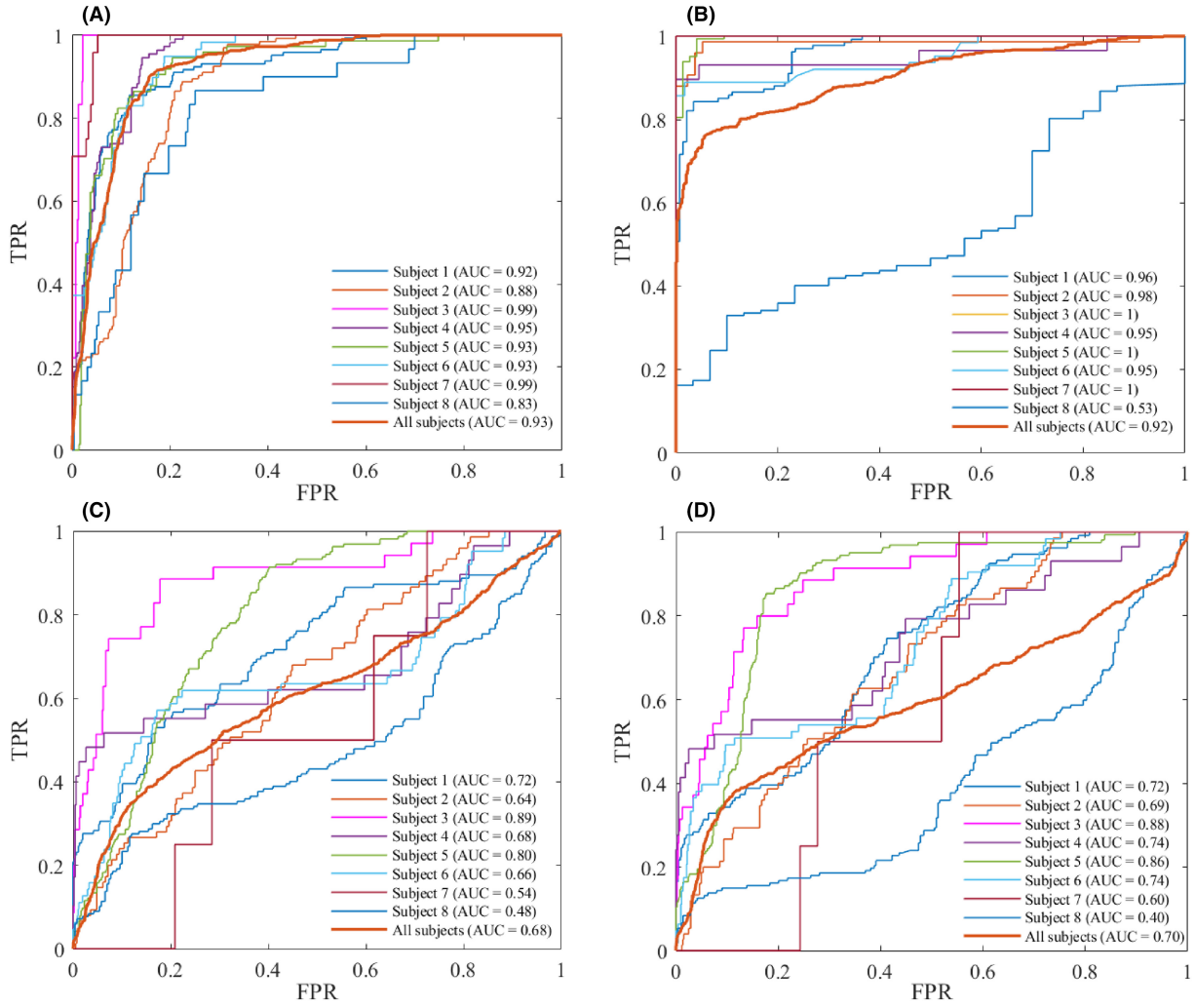

FIGURE 4 Receiver operating characteristics curves of binary sleep state classification for each subject and all subjects (aggregated results) using all features and extremely randomised trees classifier: (A) between active sleep and quiet sleep, (B) between quiet sleep and wake, (C) between active sleep and wake and (D) between sleep (including active sleep and quiet sleep) and wake. AUC values are presented for each subject and all subjects. AUC, aera under the curve; FPR, false positive rate; TPR, true positive rate.

infant had no large gross body movement during wake, which led to the absence of strong motion artefacts in their ECG or chest impedance. This means that using motion features was ineffective in distinguishing wake epochs from sleep. Notably, subject eight had a much lower kappa value (0.19) than the other subjects. Figure 4 shows that the receiver operating characteristics curve for this subject performed poorly in distinguishing between wake, active sleep and quiet sleep. A closer look at the video data revealed that this infant seemed to display a lot of sucking activity along with head and torso movements during sleep. These created motion artefacts in the ECG and chest impedance signals and the sleep epochs in those instances may have been easily misclassified as wake stages. In general, the existence of significant between-subject variability in cardiorespiratory physiology during sleep[29] limited the generalisability of the model, particularly when using a small dataset for training.

Preterm infants typically move considerably during sleep. In the early stages of their lives, they spend a lot of time in active sleep. They exhibit a lot of movement during this sleep state, including twitching, jerking and stretching.[9] Movement type is a key indicator of the sleep state of an infant.[26] Fine or subtle movements, such as eye, facial and finger movements, are rarely transmitted as motion artefacts in measured physiological signals, as this would lead to an imprecise estimation of real body movements. Thus, the direct measurement and quantification of body movement is desirable. Based on the findings of previous studies,[16,30] video-based technology may be sufficient for this purpose. Compared with a noninvasive mattress, a video can capture more subtle movements, such as limb and facial expressions.

4.1 | Strengths and limitations

The strength of this study was that we used cardiorespiratory signals obtained through routine monitoring. We extracted novel features from these signals and integrated them with existing

features to classify sleep among preterm infants. This approach improved the performance of sleep classification without adding extra burdens to the preterm infants. However, there were several limitations that should be addressed in future research. Reliable statistical analysis and generalisability of the model can only be achieved by larger and more diverse datasets. The limited sample size reduced the meaningfulness of the results. Future studies should aim to collect more data from neonatal intensive care units, to conduct real comparisons and perform statistical analyses. Notably, this study did not assess the effect of age on motion and subsequent studies should recruit more subjects, with a range of gestational ages, to investigate this dimension. It is also important to emphasise that estimated motion data were used in this study to extract features related to body movement. To obtain more reliable results, it could be preferable to measure and quantify body movement directly. In addition, future research should explore algorithms trained with polysomnography or amplitude-integrated electroencephalography-based sleep scoring systems, to further investigate the agreement between different scoring approaches in preterm infants.

5 | CONCLUSION

This study provides valuable insights into the classification of preterm infant sleep states, using cardiorespiratory signals and additional features. Our findings suggest that a combination of cardiorespiratory interaction and motion features, analysed using extremely randomised trees, led to improved performance in classifying sleep states. Motion features played a crucial role in detecting wake from sleep, while cardiorespiratory interaction features contributed to distinguishing between quiet sleep and other states. However, further research is needed to enhance the discrimination between active sleep and wake.

AUTHOR CONTRIBUTIONS

Dandan Zhang: Conceptualization; data curation; formal analysis; methodology; visualization; writing – original draft; writing – review and editing. **Zheng Peng:** Data curation; writing – original draft; writing – review and editing. **Shaoxiong Sun:** Writing – review and editing. **Carola van Pul:** Writing – review and editing. **Caifeng Shan:** Writing – review and editing. **Jeroen Dudink:** Writing – review and editing. **Peter Andriessen:** Supervision; writing – review and editing. **Ronald M. Aarts:** Supervision; writing – review and editing. **Xi Long:** Conceptualization; methodology; supervision; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interests to declare.

ETHICS STATEMENT

The Ethical Committee of the Máxima Medical Center approved the study and the parents of the preterm infants provided written, informed consent.

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REFERENCES

1. Graven SN, Browne JV. Sleep and brain development. Newborn Infant Nurs Rev. 2008;8(4):173-9. doi:10.1053/j.nainr.2008.10.008
2. Mirmiran M, Maas YGH, Ariagno RL. Development of fetal and neonatal sleep and circadian rhythms. Sleep Med Rev. 2003;7(4):321-34. doi:10.1053/smrv.2002.0243cae
3. Galland BC, Hayman RM, Taylor BJ, Bolton DPG, Sayers RM, Williams SM. Factors affecting heart rate variability and heart rate responses to tilting in infants aged 1 and 3 months. Pediatr Res. 2000;48(3):360-8. doi:10.1203/00006450-200009000-00017
4. Lehtonen L, Martin RJ. Ontogeny of sleep and awake states in relation to breathing in preterm infants. Semin Neonatol. 2004;9(3):229-38. doi:10.1016/j.siny.2003.09.002
5. Berry RB, Brooks R, Gamaldo C, et al. AASM scoring manual updates for 2017 (version 2.4). J Clin Sleep Med. 2017;13(5):665-6. doi:10.5664/jcsm.6576
6. De Groot ER, Bik A, Sam C, et al. Creating an optimal observational sleep stage classification system for very and extremely preterm infants. Sleep Med. 2022;90:167-75. doi:10.1016/j.sleep.2022.01.020
7. Dereymaeker A, Pillay K, Vervisch J, et al. Review of sleep-EEG in preterm and term neonates. Early Hum Dev. 2017;113:87-103. doi:10.1016/j.earlhumdev.2017.07.003
8. Calciolari G, Montirosso R. The sleep protection in the preterm infants. J Matern Fetal Neonatal Med. 2011;24(Suppl 1):12-4. doi:10.3109/14767058.2011.607563
9. Werth J, Atallah L, Andriessen P, Long X, Zwartkruis-Pelgrim E, Aarts RM. Unobtrusive sleep state measurements in preterm infants - a review. Sleep Med Rev. 2017;32:109-22. doi:10.1016/j.smrv.2016.03.005
10. Otte RA, Long X, Westerink J. A behavioral approach to annotating sleep in infants: building on the classic framework. Physiol Rep. 2022;10(3):e15178. doi:10.14814/phy2.15178
11. De Groot ER, Knoop MS, van den Hoogen A, et al. The value of cardiorespiratory parameters for sleep state classification in preterm infants: a systematic review. Sleep Med Rev. 2021;58:101462. doi:10.1016/J.SMRV.2021.101462
12. Harper RM, Schechtman VL, Kluge KA. Machine classification of infant sleep state using cardiorespiratory measures. Electroencephalogr Clin Neurophysiol. 1987;67(4):379-87. doi:10.1016/0013-4694(87)90126-x
13. Werth J, Radha M, Andriessen P, Aarts RM, Long X. Deep learning approach for ECG-based automatic sleep state classification in preterm infants. Biomed Signal Process Control. 2020;56:101663. doi:10.1016/J.BSPC.2019.101663

14. Sentner T, Wang X, de Groot ER, et al. The sleep well baby project: an automated real-time sleep–wake state prediction algorithm in preterm infants. Sleep. 2022;45(10):zsac143. doi:10.1093/sleep/zsac143
15. Zhang D, Long X, Xu L, et al. Characterizing cardiorespiratory interaction in preterm infants across sleep states using visibility graph analysis. J Appl Physiol. 2021;130(4):1015-24. doi:10.1152/japplphysiol.00333.2020
16. Long X, Espina J, Otte RA, Wang W, Aarts RM, Andriessen P. Video-based actigraphy is an effective contact-free method of assessing sleep in preterm infants. Acta Paediatr. 2021;110(6):1815-6. doi:10.1111/apa.15740
17. Schoch SF, Kurth S, Werner H. Actigraphy in sleep research with infants and young children: current practices and future benefits of standardized reporting. J Sleep Res. 2021;30(3):e13134. doi:10.1111/jsr.13134
18. Peng Z, Lorato I, Long X, et al. Body Motion Detection in Neonates Based on Motion Artifacts in Physiological Signals from a Clinical Patient Monitor. Annu Int Conf IEEE Eng Med Biol Soc. 2021;2021:416-9. doi:10.1109/EMBC46164.2021.9630133
19. Werth J, Serteyn A, Andriessen P, Aarts RM, Long X. Automated preterm infant sleep staging using capacitive electrocardiography. Physiol Meas. 2019;40(5):055003. doi:10.1088/1361-6579/ab1224
20. Fonseca P, Long X, Radha M, Haakma R, Aarts RM, Rolink J. Sleep stage classification with ECG and respiratory effort. Physiol Meas. 2015;36(10):2027-40. doi:10.1088/0967-3334/36/10/2027
21. Wijshoff RW, Mischi M, Aarts RM. Reduction of periodic motion artifacts in Photoplethysmography. IEEE Trans Biomed Eng. 2017;64(1):196-207. doi:10.1109/TBME.2016.2553060
22. Long X, Fonseca P, Aarts RM, Haakma R, Foussier J. Modeling cardiorespiratory interaction during human sleep with complex networks. Appl Phys Lett. 2014;105(20):203701. doi:10.1063/1.4902026
23. Geurts P, Ernst D, Wehenkel L. Extremely randomized trees. Mach Learn. 2006;63(1):3-42. doi:10.1007/s10994-006-6226-1
24. He H, Ma Y. Imbalanced learning: foundations, algorithms, and applications. 1st ed. Wiley-IEEE Press; 2013.
25. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33(1):159-74.
26. Yiallourou SR, Sands SA, Walker AM, Horne RSC. Maturation of heart rate and blood pressure variability during sleep in term-born infants. Sleep. 2012;1:177-86. doi:10.5665/sleep.1616
27. Pawar T, Anantakrishnan NS, Chaudhuri S, Duttagupta SP. Impact analysis of body movement in ambulatory ECG. Annu Int Conf IEEE Eng Med Biol Soc. 2007;2007:5453-6. doi:10.1109/IEMBS.2007.4353579
28. Lucchini M, Pini N, Fifer W, Burtchen N, Signorini M. Entropy information of cardiorespiratory dynamics in neonates during sleep. Entropy. 2017;19(5):225. doi:10.3390/e19050225
29. Long X, Haakma R, Leufkens TRM, Fonseca P, Aarts RM. Effects of between- and within-subject variability on autonomic cardiorespiratory activity during sleep and their limitations on sleep staging: a multilevel analysis. Comput Intell Neurosci. 2015;2015:1-17. doi:10.1155/2015/583620
30. Awais M, Long X, Yin B, et al. A hybrid DCNN-SVM model for classifying neonatal sleep and wake states based on facial expressions in video. IEEE J Biomed Health Inform. 2021;25(5):1441-9. doi:10.1109/JBHI.2021.3073632

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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