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Deep-spindle: An automated sleep spindle detection system for analysis of infant sleep spindles

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ABSTRACT

Background: Sleep spindles are an indicator of the development and integrity of the central nervous system in infants. Identifying sleep spindles manually in EEG is time-consuming and typically requires experienced experts. Automated detection of sleep spindles would greatly facilitate this analysis. Deep learning methods have been widely used recently in EEG analysis.

Method: We have developed a deep learning-based automated sleep spindle detection system, Deep-spindle, which employs a convolutional neural network (CNN) combined with a bidirectional Long Short-Term Memory (LSTM) network, which could assist in the analysis of infant sleep spindles. Deep-spindle was trained on the EEGs of ex-term infants to estimate the number and duration of sleep spindles. The ex-term EEG on channel F4-C4 was split into training (N=81) and validation (N=30) sets. An additional 30 ex-term EEG and 54 ex-preterm infant EEGs (channel F4-C4 and F3-C3) were used as an independent test set.

Result: Deep-spindle detected the number of sleep spindles with 91.9% to 96.5% sensitivity and 95.3% to 96.7% specificity, and estimated sleep spindle duration with a percent error of 13.1% to 19.1% in the independent test set. For each detected spindle event, the user is presented with amplitude, power spectral density and the spectrogram of the corresponding spindle EEG, and the probability of the event being a sleep spindle event, providing the user with insight into why the event is predicted as a sleep spindle to provide confidence in the predictions.

Conclusion: The Deep-spindle system can reduce physicians' workload, demonstrating the potential to assist physicians in the automated analysis of sleep spindles in infants.

1. Introduction

EEG is widely used by clinicians to evaluate patients' cognitive states, determine lesion sites, and classify symptoms [1,2] and is heavily used to evaluate the effect of medical and psychological treatment [3]. However, manually identifying events in EEG recording is a time-consuming task and is currently carried out by highly trained human experts [4]. Sleep spindles are frequent transitory elements occurring during non-rapid eye movement (NREM) sleep. Sleep spindles are the surface EEG manifestation of bursting activity of the reticular nucleus of the thalamus and its interactions with thalamocortical and cortical cells [5]. Research shows that children and adults have two-spindle frequencies: slow spindles, prevalent over the frontal areas, and fast sleep spindles, prevalent over the central/centroparietal areas [6,7]. It is widely accepted that two individual types of sleep spindles develop during childhood; fast spindles over more centroparietal areas and slow spindles over more anterior areas, which have different dynamics [7]. Ventura et al. [8] showed that sleep spindles in 4–5 months of age infants on fronto-central channels were predominant upon visual inspection on EEG. An individual's sleep spindle profile is unique and genetically determined [5], and has been shown to correlate with non-verbal cognitive abilities [9] and memory consolidation processes [10,11]. As the underlying brain matures so do the sleep spindles [5], showing potential as a neurodevelopmental marker and as an early indicator for diverse pathologies and neurodivergent progression [12–15]. Ujma et al. [9] point to three main aspects that complicates the study of sleep spindles: small datasets; lack of exhaustive reporting of all measured associations; and poor agreement on spindle

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detection methods used. EEG studies are a time-costly procedure leading to generally small datasets. For example, the median sample size of studies correlating sleep spindles with intelligence is 24 individuals [9]. Therefore, automatic detection is highly desirable in order to increase the availability and flexibility of EEG-based diagnosis and to reduce the burden on experts whilst accelerating the study of brain development.

Threshold-based [16] and machine learning-based [17–20] methods for sleep spindle detection methods have performed well in the past. These feature-based methods require the application of domain knowledge to create feature extractors, for example our previous work [20] used fourteen features as inputs to the random forest algorithm. However, feature estimation is a complicated and expensive process in terms of time, and expertise. Deep learning offers the advantages of requiring very little engineering by hand by reducing the task of developing a new feature extractor for each problem. Deep learning attempts to learn advanced features from data in an incremental manner, which eliminates the need for domain experts and core feature extraction. This has led to an increase in the number of studies that are using deep learning methods to explore new ways to detect sleep spindles automatically [21–23].

Deep learning methods have been developed using 11 to 30 adult sleep EEGs to detect sleep spindles [21,23], with sensitivity from 89.1% to 100%. However, these deep learning-based sleep spindle detection methods only measure the number or duration of sleep spindle events, rather than both. Additionally, a recognised limitation of deep learning methods is the disconnect between the output of the classifier and signal features which can be directly related to the underlying physical and physiological processes [24,25], making the interpretability of these deep learning-based sleep spindles detection methods difficult and potentially negatively impacting users' trust.

Deep learning offers the potential to effectively detect and analyse brain events in EEGs, but has not yet been applied to infant sleep spindles. To address this, in this study, we developed Deep-spindle, a method to detect sleep spindles in infant EEG data. The popularity of convolutional neural networks (CNN) has increased in recent years, making it a prudent choice for raw EEG input rather than a hand-engineered feature based approach. In addition, bidirectional Long Short-Term Memory (LSTM) networks have been widely used in speech and EEG analysis [26], as they can access long-distance content and two-way processing. Deep-spindle takes advantage of a CNN and bidirectional LSTM architecture. The method is trained and validated on the preprocessed EEG data of 81 and 30 ex-term born infants respectively, recorded at four months of age, with limited preprocessing of the EEGs. Deep-spindle was tested on an additional 30 ex-term and 54 ex-preterm infant EEGs, which were not used in training. The ex-preterm infants represent an at-risk group and are typical of infants that may require screening for neurodevelopmental abnormalities. There is a need for biomarkers that would assist in determining the degree of maturation of these infants that would be of prognostic value in predicting developmental outcome. Therefore, in this study, we developed an automated sleep spindle detection system for the analysis of infant sleep spindles. The main contributions of our work are as follows:

1. Deep-spindle can automatically estimate both the number and duration of sleep spindles in infant EEG data.
2. The method can readily detect sleep spindles in ex-preterm EEGs in addition to ex-term infants. This will support the use of Deep-spindle as a screening tool for ex-preterm infants, a particularly high at-risk group.
3. A visualisation of the amplitude of the detected sleep spindle event, the probability of the event being a sleep spindle event, the power spectral density (PSD) and the spectrogram of the signal is also presented, providing the user with insight into why the event is predicted as a sleep spindle in order to provide confidence in the decision.
4. Deep-spindle is freely available for academic use at http://lisda.ucd.ie/Deep-spindle/, giving users access to a deep learning-based system without the need for high-specification hardware.

The remainder of this work is organised as follows: In Section 2, we introduce related works. Dataset and methods used in this study are presented in Section 3. Section 4 shows the results of Deep-spindle. In Section 5, we discuss the impact of Deep-spindle. Finally, we make a brief conclusion, and outline the limitations of this paper and plans for future works in Section 5.

2. Related works

Research to date on the estimation of number or duration of sleep spindles in infant and adult EEG data has been limited. Most studies only measure the number or the duration of sleep spindle events, rather than both. It is difficult to apply these methods in practice. For the Deep-spindle method combining successive sleep spindle events separated by less than 1 s into a single spindle event avoided dividing spindle events across different epochs which may occur as with previously presented methods [18,27–30]. In addition, these studies define that if only part of the epoch contain sleep spindles, this epoch will be annotated as a sleep spindle event. If sleep spindles and non-sleep spindles present in the same epoch, these approaches may take both occurrences as one sleep spindle event. Therefore, they estimated the number of epochs which contain sleep spindles, rather than the 'real' number of sleep spindles [20]. Moreover, the start time, end time and the duration of the estimated sleep spindle events cannot be accurately expressed by these methods. Deep-spindle divided the EEG signal into small epochs, 0.5 s with 0.25 s overlap, reducing the problem of two sleep spindles occurring in one epoch.

Only two machine learning-based methods have been presented that detect both the number and duration of sleep spindle recordings [20,31]. The first is the method presented by Ventouras et al. [31], which trained and tested a feed-forward network using a single adult EEG recording. This method achieved sensitivity from 79.2% to 87.5% for sleep spindle number estimation. For the duration estimation, Ventouras et al. obtained the IoU of 0.37 ($\pm$0.31). We previously proposed an alternative method for estimating spindle duration and number, Spindle-AI [20], based on a random forest algorithm. Spindle-AI estimates the number and duration of sleep spindles in ex-term infant EEG data and demonstrated 93.3% to 93.9% sensitivity, 90.7% to 91.5% specificity, and 89.2% to 90.1% precision in the independent test set of ex-term infant EEG. The duration estimation of sleep spindle events in the independent test set showed a percent error of 5.7% to 7.4%. However, applying domain knowledge to the creation of feature extractors is time-consuming and expensive. Deep learning, on the other hand, allows for end-to-end problem-solving without conducting heavy preprocessing and hand-engineered features.

Most of the sleep spindle detection methods were trained and tested based on the same database [21,23,31]. However, different databases with different recording configurations and subjects may lead to differences in results when tested on an independent dataset not used during the development of the method. Whether these methods are overfitting or applicable to other EEG databases is not clear. Some studies developed the automatic sleep spindle detection methods on the publicly accessible MASS [42], and DREAMS [43] sleep EEG dataset. The MASS dataset contains 19 adult EEGs, and the DREAMS dataset contains eight adult EEGs. Jiang et al. [35] proposed a robust two-stage approach, which obtained an F1 score of 0.814 for the MASS dataset and 0.690 for the DREAMS dataset. Continuous wavelet transform with a Morlet basis function was developed by Tsanas et al. [38] to detect sleep spindles, with a sensitivity of 84% and specificity of 90% on the MASS database, and sensitivity of 76% and specificity of 92% on the DREAMS database. Kulkarni et al. [22] developed a CNN-RNN based transfer learning method, SpindleNet, which obtained a sensitivity of 90.1%, and a specificity of 96.2% on the MASS dataset. With sensitivity and specificity

Table 1
Previous work on sleep spindle detection.

Ref.	Subjects	Number	Sens (%)	Spec (%)	Prec (%)	F1
[28]	Adults	180	81.0	–	83.0	0.82
[29]	Adults	8	64.0	–	71.0	0.67
[21]	Adults	11	100	–	90.2	–
[27]	Adults	110	68.0	–	71.0	0.67
[18]	Adults	15	71.2	96.7	–	–
[32]	Adults	2	96.5	98.1	–	–
[33]	Adults	6	70.2	98.6	–	–
[34]	Adults	8	96.0	92.9	–	–
[31]	Adults	1	87.5	97.3	–	–
[30]	Adults	19	86.2	–	75.5	0.85
[30]	Adults	8	75.4	–	86.4	0.74
[35]	Adults	19	71.5	96.5	79.9	0.81
[35]	Adults	8	56.9	97.0	76.1	0.69
[22]	Adults	19	90.1	96.2	–	0.75
[22]	Adults	8	77.9	94.2	–	0.48
[36]	Adults	8	53.0	96.0	37.0	0.43
[36]	Adults	19	77.0	96.0	46.0	0.57
[37]	Adults	19	70.0	–	51.0	0.29
[37]	Adults	6	65.2	–	35.0	0.46
[38]	Adults	19	84.0	90.0	–	–
[38]	Adults	8	76.0	92.0	–	–
[39]	Children	56	88.2	89.7	–	–
[40]	Infants	1	62.9	–	–	–
[41]	Infants	2	87.7	–	91.9	–
[20]	Infants (R)	30	93.3	91.5	90.1	–
[20]	Infants (L)	30	93.9	90.7	89.2	–

R: Channel F4-C4/R-Spindle and L: Channel F3-C3/L-Spindle.

at 77.9% and 94.2%, respectively, on the DREAMS database. Daniel et al. [36] developed a sleep spindle detector, MUSSDET, based on a multivariate classification of EEG epochs. This method achieved 77.0% sensitivity, 96.0% specificity and 0.57 F1 score on the Mass database, with a sensitivity of 53.0%, specificity of 96.0% and F1 score of 0.43 on the DREAMS database. Patti et al. [37] used multivariate Gaussian mixture models to detect sleep spindles on adult EEGs, with a sensitivity of 70.0% and an F1 of 0.29 on the MASS database. For the DREAMS database, this method achieved a sensitivity of 65.2% and an F1 of 0.46. You et al. [36] proposed an adaptive U-Net framework, SpindleU-Net, to detect sleep spindle, with a sensitivity of 86.2% and F1 of 0.85 on the MASS database, the sensitivity of 75.4% and F1 of 0.74 on the DREAMS database. These approaches showed high performance on sleep spindle duration detection on a different database. However, the number of sleep spindles in the EEG recording was not presented. Additionally, most of these sleep spindle detection methods were developed using EEGs from adults [21,23,29–31]. Table 1 presented the previous work on sleep spindle detection.

3. Materials and methods

3.1. Subjects

Ethical approval was granted from the Clinical Research Ethics Committee of the Cork Teaching Hospitals, Cork, Ireland (ECM 3 04/04/17 & ECM 3 14/08/18 and ECM 4 09/05/17 & ECM 3 16/10/18) and consent from parents or guardians of the infants included in the study were obtained. EEG data were recorded from sleeping ex-term infants (N = 141) at four months. EEG (Lifelines, UK) was recorded with a sampling frequency of 500 Hz. EEG from each infant was recorded for about 70 min. An experienced clinical physiologist (expert 1) manually annotated sleep spindles of ex-term infants as the gold standard on channels F4-C4 and channel F3-C3 with duration markers (Fig. 1). In the following text we refer to the sleep spindles on channel F4-C4 as "R-Spindle" and the sleep spindles on channel F3-C3 as "L-Spindle". An additional, 54 ex-preterm infants born at 32–36+6 weeks gestational age were recruited that had an EEG recorded at four months adjusted age, with sampling rate at 500 Hz. An approximately 30 min epoch was extracted from the ex-preterm EEG based on the period where sleep spindles were manually annotated by an experienced research nurse (expert 2) as the gold standard on channels F4-C4 and F3-C3.

Table 2
The number and duration of the sleep spindles in the EEGs used in this study.

	Channel F4-C4		Channel F3-C3	
	Ex-T	Ex-P	Ex-T	Ex-P
Infants No.	141	54	141	54
Avg SS No./infant	167	105	155	110
Avg dur/SS	3.09	3.08	3.04	2.98
Total SS No.	23,520	5644	21,815	5928
Total SS dur (s)	67,997	17,394	66,320	17,676
Total non-SS dur (s)	509,535	54,357	511,212	54,075

Avg: average; No.: number; dur: duration; SS: sleep spindle; Ex-T: ex-term; Ex-P: ex-preterm.

To train Deep-spindle we used channel F4-C4 from 81 of the 141 pre-processed ex-term infant EEGs. Another channel F4-C4 of 30 independent ex-term infant EEG recordings were used to validate the method. The remaining 30 ex-term and an additional 54 ex-preterm infants EEG recordings on channel F4-C4 and channel F3-C3 were used for independent testing of Deep-spindle. Additionally, the publicly available DREAMS [43] adults EEG dataset was also used as the independent test set (See Supplementary data). The number and duration of the sleep spindles in the EEGs used in this study are presented in Table 2.

3.2. Classification algorithm of deep-spindle

The raw EEG signals were first filtered with a 50 Hz notch filter to remove powerline interference, and the DC offset was removed from each channel. In order to increase the precision of the start time and duration of the detected sleep spindles, the pre-processed EEG signal recorded on channel F4-C4 and F3-C3 was segmented into 0.5 s epochs with 0.25 s overlap, as the minimum required length of a sleep spindle is 0.5 s [44]. The Deep-spindle architecture, which employs a CNN combined with a bidirectional LSTM network is presented in Fig. 2.

The complete network comprised a time distributed layer of the complete CNN structure. The first layer of the CNN consists of frames distributed in time. The input for the Deep-spindle system consisted of a single-channel EEG signal with a moving window of length 0.5 s (with 0.25 s overlap). The input thus consists of a 250 element vector containing the EEG time series (0.5 s × 500 Hz). The CNN comprised six 1D convolutions each followed by a rectified linear unit (ReLU) activation [45]. In preliminary work we experimented with increasing and decreasing the number of convolutional layers of the CNN architecture, the best performance was observed with the current architecture as presented here (See Supplementary data). The max-pooling and spatial dropout layers were situated after every two 1D convolutions. Spatial dropout was used to help improve independence between features [46]. Then global max pooling and a 0.01 drop out layer followed the last two 1D convolutions. Two bidirectional LSTM layers were followed by a dense layer with ReLU activation and the number of units in the bidirectional LSTM was set to 100. A dropout layer of 0.5 was followed by the first and the second bidirectional LSTM layers. In the last layer a softmax activation was used. We chose stochastic gradient descent optimisation for the optimiser with a learning rate of 0.01, a decay rate of 0.0001 and a momentum of 0.8.

Post-processing: Rodenbeck et al. [44] proposed that the length of 0.5 s is the minimum required length of a sleep spindle [44]. Therefore, if the duration of a predicted sleep spindle was not greater than 0.5 s, the event was re-labelled as a non-sleep spindle event. Otherwise, it was labelled as a sleep spindle event. After filtering for the duration of the predicted sleep spindles; the number, start time, end time, and the duration of each estimated sleep spindle event in the EEG recordings was estimated.

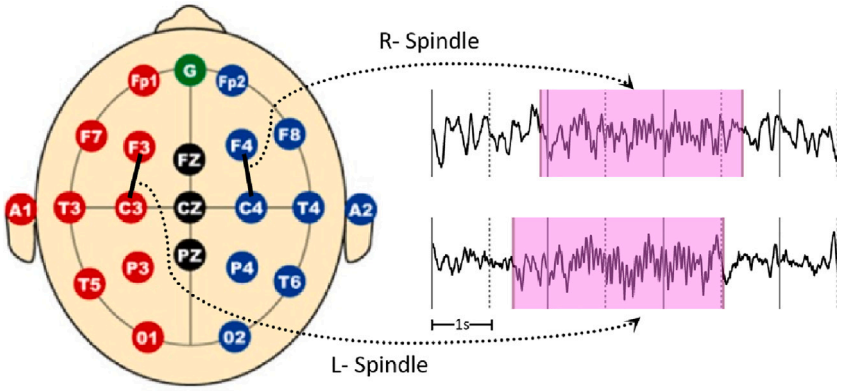

Fig. 1. Channels of EEG recording used in this study (the signal in shaded block indicates the presence of a sleep spindle event).

3.3. Implementation and data visualisation

To qualify as a sleep spindle event, the EEG must show a primary frequency between 12 and 14 Hz and must be clearly visible from the background activity [47]. Deep-spindle presents the number of sleep spindles and the start time, duration and end time of each detected sleep spindle event in each EEG recording channel. In addition, Deep-spindle can display an image of each detected sleep spindle event, the probability of the event being a sleep spindle event, corresponding PSD from 0 Hz to 30 Hz, and the spectrogram of the signal (Fig. 5). Moreover, we visualised 1 s of activity before and after the detected sleep spindle events to help users compare the spectrogram of the signal, amplitude and probability of sleep spindle events and non-sleep spindle events. The PSD analysis and the spectrogram of the signal mimics how physicians detect whether the activity is a sleep spindle event or not, rather than merely providing an explanation of the logical concepts behind the "black box" [48–51].

The Deep-spindle approach was implemented in Python 3.6.5 [MSC v.1900 64 bit (AMD64)] with Keras API and TensorFlow (version 1.14.0) backend, and IPython 6.4.0 in Jupyter notebook v.4.4.0 from Anaconda. It took approximately 9 h to train the Deep-spindle approach, and approximately 1 min to test the result for each infant. The approach was run on the Windows 10 DESKTOP consisting of Intel(R) Core(TM) i7-7700HQ CPU (4 cores) and an NVIDIA GeForce GTX 1050 TI GPU. Deep-spindle allows users to upload EEG data and returns the start and end times of detected sleep spindle events along with the corresponding PSD and spectrogram. It took approximately 30 s to analyse 5100 s data. Deep-spindle is an automated deep learning-based system that aims to provide a safe and effective platform to assist physicians to annotate and analyse infants' sleep spindles (See Fig. 3 and Supplementary data). There is no requirement for computer programming skills or installation of any software or system.

3.4. Performance evaluation

To measure the agreement the annotated data from experts 1 and 2 were compared. Sleep spindles from two channels (channel F4-C4 and F3-C3) in 65 of 141 ex-term infants EEGs during the first sleep cycle (around 58 ± 23 min in each EEG) were annotated by expert 1 and expert 2. Cohen's kappa was estimated to measure inter-rater reliability between the two (Table 3). In addition, Cohen's kappa was estimated to measure the performance of the Deep-spindle method to compare the reliability of the Deep-spindle method with that of experts.

$$P_0 = \frac{A+D}{A+B+C+D} \tag{1}$$

$$P_e = \frac{A+B}{A+B+C+D} \times \frac{A+C}{A+B+C+D} + \frac{C+D}{A+B+C+D} \times \frac{B+D}{A+B+C+D} \tag{2}$$

Table 3
Cohen's kappa coefficient between two experts.

Channel	EP	SS No.	Both No.	kappa	STD	SEM
F4-C4	1 2	8165 8195	7254	0.820	0.080	0.010
F3-C3	1 2	8045 8203	7146	0.804	0.090	0.011

EP: Expert; SS No.: Number of sleep spindles labelled by each expert; Both No.: Number of sleep spindles labelled by both experts. kappa: Cohen's kappa coefficient; STD: standard deviation; SEM: Standard error of the mean.

$$K = \frac{P_0 - P_e}{1 - P_e} \tag{3}$$

where: A is an event labelled as a sleep spindle by expert 1 and expert 2. B is an event labelled as a sleep spindle by expert 1 but labelled as a non-sleep spindle by expert 2. C is an event labelled as a sleep spindle by expert 2 but labelled as a non-sleep spindle by expert 1. D is an event labelled as a non-sleep spindle event by expert 1 and expert 2. P_0 is proportion of the agreements between expert 1 and expert 2. P_e is proportion of the agreements between expert 1 and expert 2 would be expected by chance.

Sleep spindle number estimation

The sensitivity (Sens), specificity (Spec), precision (Prec), accuracy (Acc) and Matthews correlation coefficient (MCC) of Deep-spindle in estimating the number of sleep spindle events were evaluated [20]. Moreover, F1 score (F1) was also used to evaluate Deep-spindle.

$$F1 = 2 * \frac{Sens * Prec}{Sens + Prec} \tag{4}$$

Sleep spindle duration estimation

The duration of sleep spindles estimated by Deep-spindle in the EEG recording was evaluated using the percent error on individual infant EEGs. Percent error was calculated as in [20].

4. Results

4.1. Inter-rater reliability

Table 3 presents the Cohen's kappa coefficient between the two experts, which was greater than 0.80 in both sets of infant EEG recordings.

Table 4 presents Cohen's kappa coefficient between experts and the Deep-spindle method for the exterm and ex-preterm infant EEGs.

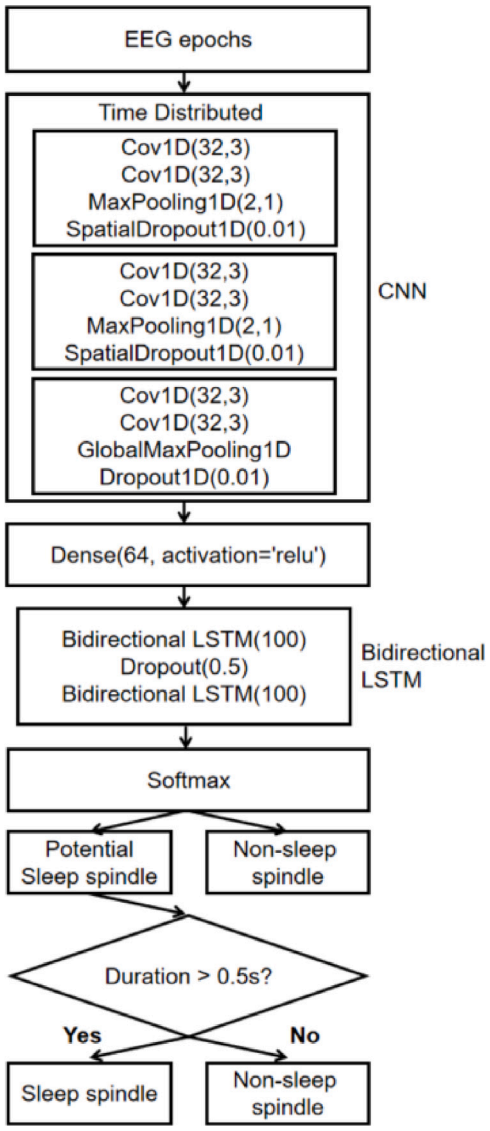

Fig. 2. Overview of Deep-spindle: Deep learning-based infant sleep spindle detection method. Deep-spindle combines a CNN and bidirectional LSTM network. The preprocessed input EEG data is processed by a three layers CNN which acts as a feature extractor. The input for the Deep-spindle system consisted of a single-channel EEG signal with a moving window of length 0.5 s (with 0.25 s overlap). For 0.5 s EEG with 500 Hz sampling frequency, the length of the input vector is 250 samples. The batch size is 64, and the epoch is set to 100. The features learned by the CNN then feed into the LSTM. The LSTM consists of 100 bidirectional LSTM cells. A softmax activation function was used to predict the potential sleep spindle events and non-sleep spindle events. The duration of the potential sleep spindle events were then further examined before classification as sleep spindles or non-sleep spindles.

4.2. Performance in estimating the number of sleep spindles

An example of representative F4-C4 EEG signals from a exterm infant illustrating sleep spindle events is presented in Fig. 4. The raw signal, with the output of the Deep learning algorithm and final predicted sleep spindle events are shown.

Table 5 presents the performance of Deep-spindle at estimating the number of spindles in the training, validation, and independent test sets. The result of counting the number of sleep spindles in the ex-term independent test set on channel F4-C4 and F3-C3, which were not used in training, obtained a sensitivity and specificity of 92.5%–95.5% and 95.3%–96.1%, respectively. Deep-spindle achieved an F1 score from 0.924–0.947 for the independent test set. For the ex-preterm infant EEG data Deep-spindle achieved sensitivity, specificity and F1 score of 91.9%–96.5%, 96.1%–96.7% and 0.935–0.954, respectively for both channels.

Table 4
Cohen's kappa score between the experts' annotations and the Deep-spindle method.

Dataset	Channel	Both No.	kappa	STD	SEM
Ex-term	F4-C4	20,592	0.836	0.116	0.010
	F3-C3	20,439	0.828	0.122	0.010
Ex-preterm	F4-C4	5378	0.821	0.076	0.010
	F3-C3	5369	0.790	0.105	0.014

Both No.: Number of sleep spindles labelled by both experts and Deep-spindle; kappa: Cohen's kappa score; STD: standard deviation; SEM: Standard error of the mean.

4.3. Performance in duration estimation of sleep spindles

Table 6 presents the performance of the sleep spindle duration estimation by Deep-spindle. The mean duration of each sleep spindle labelled by expert 1 was 3.20 s on channel F4-C4 and 3.08 s on channel F3-C3 of the ex-term infants' independent test set. Compared with expert annotation, Deep-spindle estimated the mean duration of sleep spindles as 2.66 s and 2.50 s on the channel F4-C4 and F3-C3, respectively, with a percent error of 17.0% (channel F4-C4) and 19.1% (channel F3-C3). For the ex-preterm infant EEG data, expert 2 annotated 3.12 s on channel F4-C4, 3.04 s on channel F3-C3. Deep-spindle detected each sleep spindle's mean duration with 2.72 s and 2.60 s on channel F4-C4 and F3-C3, respectively, with an error of 13.1%–15.6% in ex-preterm infant EEG.

4.4. Implementation and data visualisation

Fig. 5 presents the amplitude, probability of the event being a sleep spindle events (Fig. 5(C)), corresponding PSD (Fig. 5(A)) and the spectrogram (Fig. 5(B)) of a detected sleep spindle event. There is a clear peak in the 12–14 Hz range, Fig. 5(A). Fig. 5(B) confirms that the sleep spindle events contain elevated power in the 12–14 Hz region between 566 and 569.5 s. Fig. 5 is automatically saved for each detected sleep spindle event, allowing the user to identify the epochs identified as spindle events by Deep-spindle and quickly check the accuracy of the detected sleep spindles. Fig. 6 presents the mean absolute amplitude of the TP/FP/TN/FN events in ex-term and ex-preterm infants.

5. Discussion

In this study, we developed an automated sleep spindle detection method, Deep-spindle, for analysis and visualisation of infant sleep spindles. Deep-spindle can automatically estimate the number and duration of sleep spindles in infant EEG data. Previous methods for infant and adult sleep spindle detection require the application of domain knowledge for the creation of feature extractors [21,22,52], which is a complicated and expensive process in terms of time, and expertise [53]. Deep-spindle used raw EEG data as input without requiring any heavy preprocessing, domain expertise or core feature extraction.

From Table 5 we can see that the MCC in the ex-term infants on channel F4-C4 (R-SS) was 0.914, and the MCC for the ex-term on channel F3-C3 (L-SS) was 0.878 on the independent test set. MCC on channel F4-C4 was 0.036 higher than that of the channel F3-C3. For the ex-preterm infants sleep spindle, the MCC on channel F4-C4 (0.922) was 0.035 higher than MCC on channel F3-C3 (0.887). The error for the estimated spindle duration was similarly lower on channel F4-C4 than on channel F3-C3 for both the ex-term. One of the reasons why the MCC and percent error on channel F4-C4 performs better than that of the channel F3-C3 may be that the model was trained on the F4-C4 channel, and the sleep spindle events on channel F4-C4 are slightly different from that on channel F3-C3. Even though the EEG signals

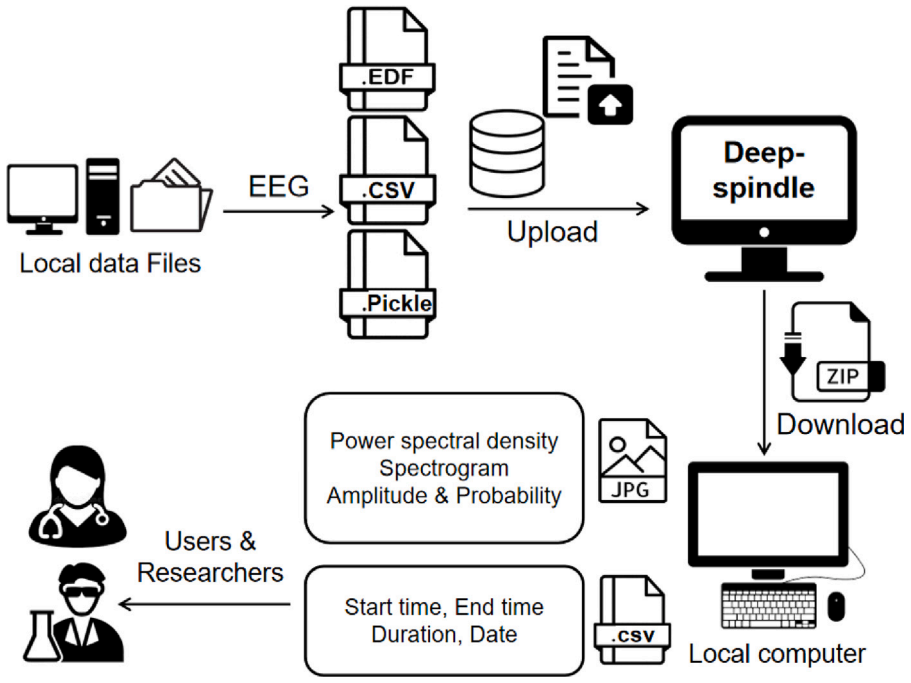

Fig. 3. The Deep-spindle system. There is no requirement for computer programming skills or installation of any software or system. The workflow of Deep-spindle contains (1) organising and uploading local EEG data files (EDF, CSV or Pickle format) to Deep-spindle, (2) waiting for the results provided by Deep-spindle (3) checking and downloading results to a personal computer. Start time, end time and duration of each predicted sleep spindle events can be found in the CSV file. The amplitude, the probability of the event being a sleep spindle event, the corresponding PSD from 0 Hz to 30 Hz, and the spectrogram of the sleep spindle event estimated by Deep-spindle are presented in the JPG file.

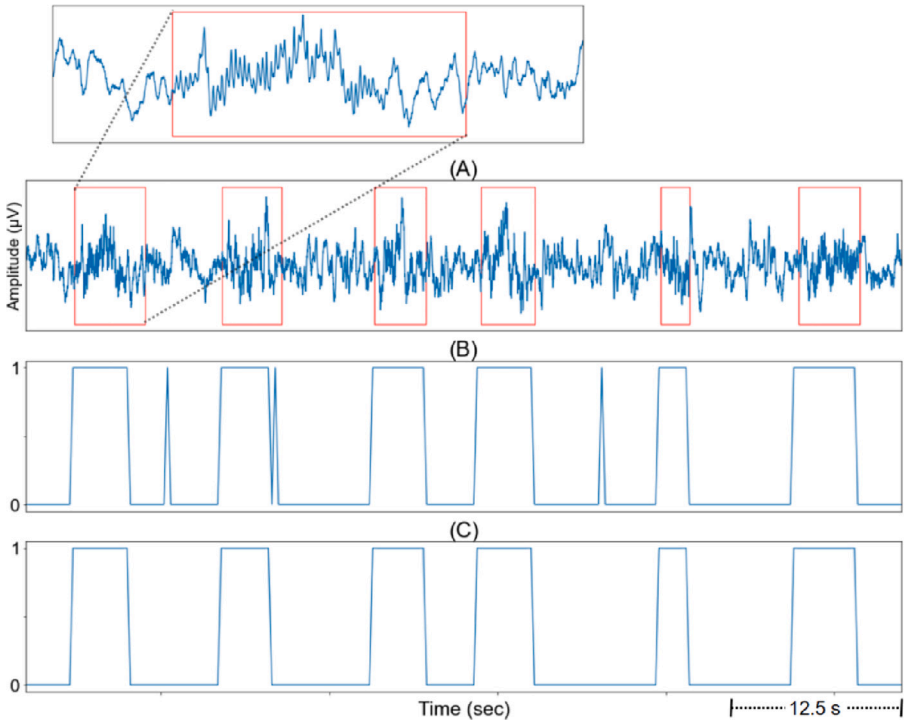

Fig. 4. Post-processing: (A) Original signal on channel F4-C4 of exterm infant's EEG (the signal in the red block indicates the presence of a sleep spindle event); (B) Sleep spindles detected by CNN-bidirectional LSTM algorithm; (C) Sleep spindles detected by Deep-spindle with post-processing.

between the channels are highly correlated, there are subtle differences between the two.

Fig. 6 shows that the amplitude of the EEG signals for epochs identified as FPs and FNs were higher than the TNs and TPs. It may because the FPs and FNs are contaminated with noise or artefact, such as movement artifact. Fig. 5 presents the amplitude, probability of the event being a sleep spindle event, corresponding PSD and spectrogram of a detected sleep spindle event. This provides physicians with context about why a decision is made and a more detailed view into what may be going on in the EEGs and may increase confidence in using Deep-spindle clinically.

Table 5
Performance of sleep spindle number estimation by Deep-spindle on ex-term and ex-preterm infant EEG data.

	Dataset	Actual	Automatic	TP	FN	FP	TN	Sens (%)	Spec (%)	Prec (%)	F1	MCC
	Train (N = 81)	13,463	13,016	12,368	1095	648	17,562	93.0	97.0	95.5	0.942	0.903
R	Val (N = 30)	4304	4418	4127	177	297	5978	96.8	95.9	93.6	0.952	0.920
	Test (N = 30)	4263	4322	4097	167	225	5561	95.5	96.1	93.9	0.947	0.914
L	Ex-T (N = 30)	4252	4262	3983	269	279	5541	92.5	95.3	92.4	0.924	0.878
R	Ex-P (N = 54)	5644	5697	5378	266	319	7268	96.5	96.1	94.4	0.954	0.922
L	Ex-P (N = 54)	5928	5637	5369	559	268	7236	91.9	96.7	95.2	0.935	0.887

R: Channel F4-C4/R-Spindle; L: Channel F3-C3/L-Spindle; Actual: The sleep spindles annotated by experts; Automatic: The sleep spindles predicted by Deep-spindle. Train: training; Val: Validation; Ex-T: Ex-term; Ex-P: Ex-preterm.

Table 6
Performance of sleep spindle duration estimation by Deep-spindle on ex-term and ex-preterm infant EEG data.

	Dataset	Act dur (± std) (s)	Est dur (± std)	Mean of error (± std) (s)	Percent error (± std) (%)
	Training (N = 81)	3.08 (± 0.60)	2.59 (± 0.62)	0.49 (± 0.31)	16.2 (± 10.2)
R	Validation (N = 30)	3.07 (± 0.52)	2.58 (± 0.49)	0.49 (± 0.30)	15.7 (± 08.5)
	Test (N = 30)	3.20 (± 0.55)	2.66 (± 0.55)	0.55 (± 0.34)	17.0 (± 10.0)
L	Ex-term (N = 30)	3.08 (± 0.59)	2.50 (± 0.62)	0.58 (± 0.36)	19.1 (± 11.8)
R	Ex-preterm (N = 54)	3.12 (± 0.53)	2.72 (± 0.53)	0.41 (± 0.31)	13.1 (± 09.7)
L	Ex-preterm (N = 54)	3.04 (± 0.58)	2.60 (± 0.58)	0.48 (± 0.39)	15.6 (± 11.9)

R: Channel F4-C4/R-Spindle; L: Channel F3-C3/L-Spindle; Act dur: mean actual sleep spindle duration annotated by experts; Est dur: mean estimated sleep spindle duration by Deep-spindle.

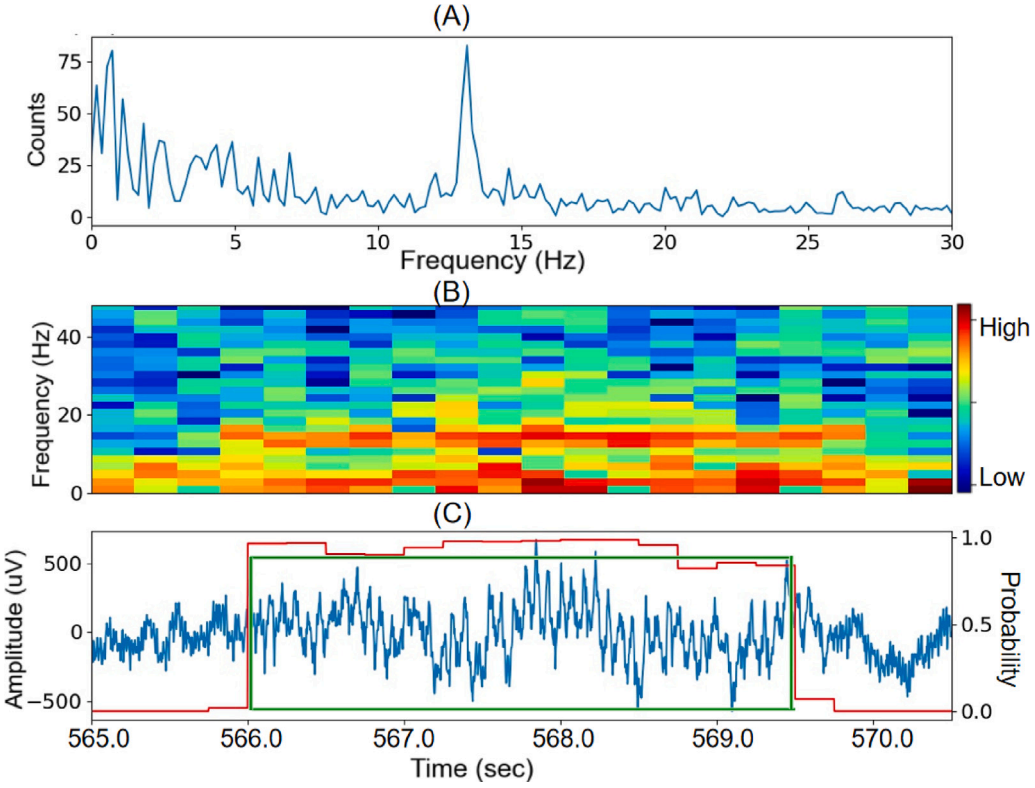

Fig. 5. Data visualisation of detected sleep spindle event: (A) PSD, (B) spectrogram and (C) amplitude of the sleep spindle event estimated by Deep-spindle. The signal in the green block indicates the presence of a sleep spindle event, the red line represents the probability of the event being the sleep spindle events detected by the algorithm.

Sleep spindles have been shown to change with ageing [54] possibly reflecting maturation changes such as synapses generation and elimination, and myelination [55]. The rapid development of the infant brain, and the variability in sleep spindles makes infant sleep spindle detection challenging. Therefore, an infant-specific algorithm is much called-for. In our previous work [20], we demonstrated that adult sleep spindles detection methods may not be suitable for infant sleep spindle detection, highlighting the importance of an infant-specific sleep spindle detection algorithm (See Supplementary data). Deep-spindle was trained on ex-term infant EEG data, however, it can estimate sleep spindle events not only in ex-term infant EEG, but also in ex-preterm infant EEG recordings. Sleep spindles have the potential to be used as markers of typical/atypical brain maturation. The ex-preterm infants represent an at risk group who would benefit from the availability of a neurodevelopmental marker to assist with early screening for neurodevelopmental abnormalities. Deep-spindle has the advantage of including late-preterms, which is a well-known risk group for atypical neurodevelopment [56]. The results of Deep-spindle show that Deep-spindle can readily detect both the number and duration of sleep spindle events in the EEG recordings of ex-preterm infants. Deep-spindle will hopefully provide the foundations the establishment of early risk detection measures for early intervention.

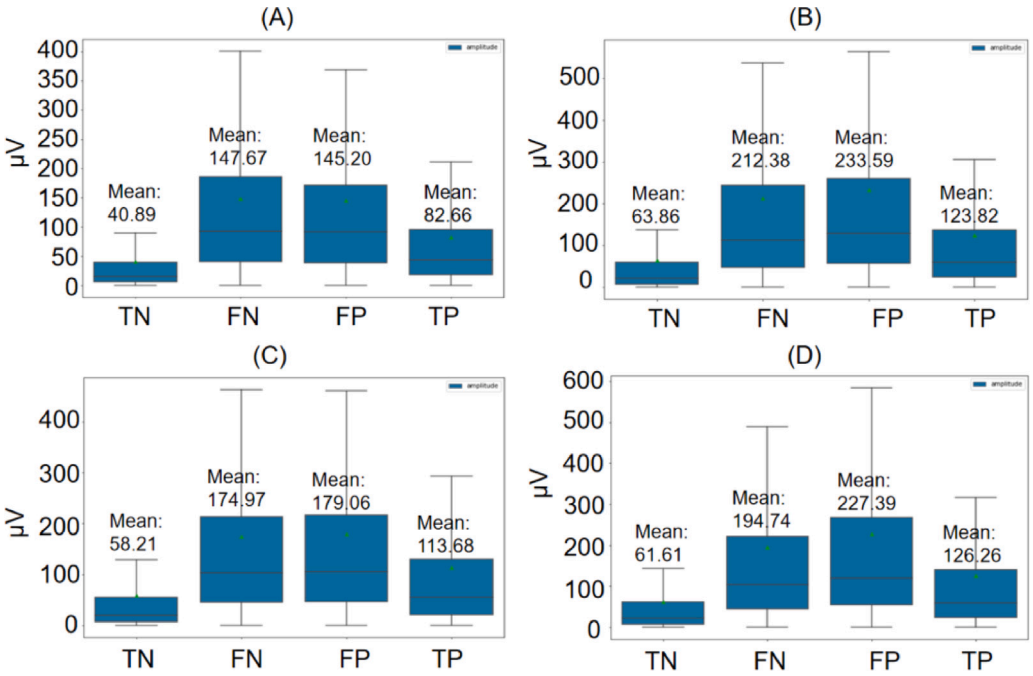

Fig. 6. Mean absolute amplitude of EEG events (TN/FN/FP/TP) in (A) Ex-term infants (R-spindle) (B) Ex-preterm infants (R-spindle) (C) Ex-term infants (L-spindle) (D) Ex-preterm infants (L-spindle).

Overall, manual identification of sleep spindles by experts in EEG recordings is time-consuming and subject to inter-rater variability, as expert human reviewers do not always agree [57]. In this study, we did compare the annotations between expert 1 and 2, and the kappa score was high. Table 3 presents the kappa score between expert 1 and 2. The kappa score shows strong agreement between the two experts, but there are differences between expert annotations (the kappa score is not equal to 1). Deep-spindle is trained on the manual annotation of experts, hence, the predictions cannot be superior to experts. However, Deep-spindle will always assign similar annotations to the sleep spindles, enabling the objective detection of sleep spindles in EEG recordings and reducing preference differences and variability among experts. This is an advantage over manual scoring, as after training, automatic annotation is not subject to factors such as human error, human preference, label environment, or the level of vigilance [58]. The infant sleep spindles annotated by Deep-spindle have a high consistency with expert annotation (Cohen's kappa coefficient around 0.8), which is similar to the variability between our two expert annotations (Cohen's kappa coefficient around 0.8). Another advantage over manual scoring is that the sleep spindle events of each infant EEG recording could be estimated in less than a second by Deep-spindle, whereas manually annotated by experienced experts could take hours.

In this study, when the physicians reviewed the probability of detected sleep spindle events that Deep-spindle learned on its own, it showed that what Deep-spindle learned "made sense" in terms of our understanding of these events. The higher probability sections may actually represent factors associated with sleep spindles, providing a basis for further research. In addition, the corresponding PSD and spectrogram can be visualised for the events predicted as sleep spindle events, which may help to gain users trust in the system and assist experts analysis of infant sleep spindles. We believe that this will enhance the probability of Deep-spindle being used in clinical practice and facilitate more extensive validation in a clinical setting.

6. Conclusion and future work

In this study, we described an automated deep learning-based system for infants' sleep spindle analysis, Deep-spindle, which automatically detects sleep spindles in infant EEG recordings using a single-channel infant EEG as the input. Deep-spindle was tested in a large dataset recorded from 141 ex-term infants and 54 ex-preterm infants, which achieved 91.9% to 96.5% sensitivity, 95.3% to 96.7% specificity and 0.924 to 0.954 F1 score for sleep spindle number detection. Sleep spindle duration was estimated with an error of 13.1% to 19.1% in the independent test set. High accuracy was also achieved on ex-preterm infant EEG recordings which were not used in training. The method presented will allow a faster, more reliable, and more reproducible detection of infant sleep spindles based on single-channel EEG analysis. The Deep-spindle system presents the start and end times of sleep spindles in long EEG recordings, and the amplitude, probability of the event being a sleep spindle event, PSD and spectrogram of any detected sleep spindle, which will assist physicians and researchers in the analysis of infant sleep spindles. We expect that Deep-spindle can be widely used in various clinical environments to save time and the effort of manual annotation.

In considering the limitations of the approach it should be noted that the percent error of the duration estimation from Deep-spindle is higher than our previous approach using random forest-based machine learning trained on features identified by experts with domain knowledge [20]. Additionally, in this work we did not remove motion artefacts, which are present in infant studies, though minimal in NREM sleep when the sleep spindles occur. These can be removed through additional pre-processing steps or high-pass filtering if necessary. In addition the datasets used to train and test in this study were recorded by the same EEG system. The performance of Deep-spindle on a dataset recorded from other EEG systems with a different sampling frequency is unclear. However, once the data have a similar signal to noise ratio and are recorded at frequencies above the Nyquist frequency, similar performance would be expected. In future work, it would be valuable to evaluate how Deep-spindle performs in datasets recorded by other EEG systems. Moreover, we will check whether Deep-spindle works well on children's sleep EEG recordings.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary material related to this article can be found online at https://doi.org/10.1016/j.compbiomed.2022.106096.

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