Cuadernos de Neuropsicología / Panamerican Journal of Neuropsychology
2026, Vol. 20 Nº 2 154 - 170

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

DYNAMICS OF SLEEP SPINDLES IN CHILDREN WITH DOWN SYNDROME: A PILOT STUDY OF ELECTROENCEPHALOGRAPHIC MICROARCHITECTURE

DINÁMICA DE LOS HUSOS DE SUEÑO EN NIÑOS CON SÍNDROME DE DOWN: UN ESTUDIO PILOTO DE MICROARQUITECTURA ELECTROENCEFALOGRÁFICA

DINÂMICA DOS FUSOS DO SONO EM CRIANÇAS COM SÍNDROME DE DOWN: UM ESTUDO PILOTO DE MICROARQUITETURA ELETROENCEFALOGRÁFICA

RECIBIDO: *31 diciembre 2025* ***ACEPTADO:*** *26 marzo 2026*

*María Olga Retamal [1] *J. Amaro-Fuenzalida [2] Tomás Mesa Latorre [3] Jovita Corzo Lameiro [1]
Tomás Ossandón Valdés [2] Juan Pablo Retamal Rosales [4] Gregorio Sierra Del Villar [5]

1. Pediatric Neurology. Fellow in Pediatric Sleep Medicine Pontificia Universidad Católica de Chile
2. Laboratory of Neurodynamics of Cognition. Pontificia Universidad Católica de Chile
3. Pediatric Neurology. Pontificia Universidad Católica de Chile
4. Independent Researcher, Santiago, Chile.
5. Pediatric Neurology Universidad de Antioquia de Colombia. Fellowship in Pediatric Sleep Medicine Pontificia Universidad Católica de Chile

A B S T R A C T

Objective: To characterize the topographic distribution, density, and interhemispheric synchrony of sleep spindles in children with Down syndrome using retrospective analysis of polysomnographic data. **Methods:** Polysomnographic recordings from 13 children with Down syndrome were analyzed. Spindle detection was performed using bandpass filtering, Hilbert transform, and amplitude thresholding during N2 sleep. Spindle density, symmetry between hemispheres, and topographic patterns were assessed. **Results:** Children with Down syndrome exhibited increased slow-wave sleep (N3) and reduced REM sleep compared to normative values. Sleep spindles showed a predominance in posterior and left-hemisphere regions. Fast spindles (14–16 Hz) were more densely distributed than slow spindles (10–13 Hz), and statistical differences in spindle density were found across channels. Interhemispheric synchrony was moderate but not statistically significant. **Conclusions:** Alterations in sleep spindle architecture and distribution were observed in children with Down syndrome. These findings suggest a potential link between spindle patterns and neurodevelopmental processes in this population, warranting further investigation.

Keywords: Down syndrome; Sleep spindles; EEG; neurodevelopment; Polysomnography.

Palabras clave: *síndrome de Down; husos del sueño; EEG; neurodesarrollo; polisomnografía.*

Palavras-chave: *síndrome de Down; fusos do sono; EEG; neurodesenvolvimento; polissonografia.*

Correspondencia: María Olga Retamal Rosales. Email: dramoretamalneuroinfantil@gmail.com . Castellón 1370, departamento 301, Torre A, Concepción. Chile.

* These authors contributed equally to this work as first authors.

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

R E S U M E N

Objetivo: Caracterizar la distribución topográfica, la densidad y la sincronía interhemisférica de los husos de sueño en niños con síndrome de Down mediante un análisis retrospectivo de registros polisomnográficos. **Métodos:** Se analizaron registros polisomnográficos de 13 niños con síndrome de Down. La detección de husos se realizó mediante filtrado pasa-banda, transformada de Hilbert y umbralización de amplitud durante el sueño N2. Se evaluaron la densidad de husos, la simetría entre hemisferios y los patrones topográficos. **Resultados:** Los niños con síndrome de Down presentaron un aumento del sueño de ondas lentas (N3) y una reducción del sueño REM en comparación con valores normativos. Los husos de sueño mostraron una predominancia en regiones posteriores y del hemisferio izquierdo. Los husos rápidos (14–16 Hz) se distribuyeron con mayor densidad que los husos lentos (10–13 Hz), y se observaron diferencias estadísticas en la densidad de husos entre canales. La sincronía interhemisférica fue moderada, pero no alcanzó significación estadística. **Conclusiones:** Se observaron alteraciones en la arquitectura y distribución de los husos de sueño en niños con síndrome de Down. Estos hallazgos sugieren una posible relación entre los patrones de husos y los procesos del neurodesarrollo en esta población, lo que justifica futuras investigaciones.

R E S U M O

Objetivo: Caracterizar a distribuição topográfica, a densidade e a sincronia inter-hemisférica dos fusos do sono em crianças com síndrome de Down, por meio de uma análise retrospectiva de dados polissonográficos. **Métodos:** Foram analisados registros polissonográficos de 13 crianças com síndrome de Down. A detecção dos fusos foi realizada utilizando filtragem pass a-banda, transformada de Hilbert e limiarização de amplitude durante o sono N2. Foram avaliadas a densidade dos fusos, a simetria entre hemisférios e os padrões topográficos. **Resultados:** Crianças com síndrome de Down apresentaram aumento do sono de ondas lentas (N3) e redução do sono REM em comparação com valores normativos. Os fusos do sono mostraram predominância em regiões posteriores e no hemisfério esquerdo. Fusos rápidos (14–16 Hz) foram mais densamente distribuídos do que fusos lentos (10–13 Hz), e foram encontradas diferenças estatisticamente significativas na densidade dos fusos entre os canais. A sincronia inter-hemisférica foi moderada, mas não estatisticamente significativa. **Conclusões:** Foram observadas alterações na arquitetura e na distribuição dos fusos do sono em crianças com síndrome de Down. Esses achados sugerem uma possível relação entre os padrões de fusos e os processos de neurodesenvolvimento nessa população, justificando investigações adicionais.

Sleep is a fundamental, cyclical, and reversible physiological state, characterized by a transient loss of consciousness and reduced responsiveness to external stimuli. This process involves dynamic changes in neuronal activity and neuroendocrine functions that are essential for brain development and maintenance (Zhu & Zee, 2012). Despite occupying nearly one-third of the human lifespan, the precise functions of sleep remain incompletely understood, particularly in populations with neurocognitive conditions.

Among the various electrophysiological features that define sleep architecture, sleep spindles—oscillatory bursts in the 11–16 Hz range lasting at least 0.5 seconds—have drawn attention for their role in synaptic plasticity, memory consolidation, cortical maturation, and other higher-order cognitive processes (American Academy of Sleep Medicine, 2007; Ulrich, 2016). Their presence, density, and synchrony are thought to reflect the functional state of the central nervous system, positioning them as potential biomarkers of neurodevelopment and neuropsychiatric disorders such as schizophrenia, autism spectrum disorder, and intellectual disability (Gruber & Wise, 2016; Chatburn et al., 2020; Au & Harvey, 2020).

Down syndrome (DS), most often caused by trisomy of chromosome 21, is the most prevalent genetic cause of intellectual disability (Sommer & Henrique-Silva, 2008). Children with DS frequently display an altered sleep

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

architecture characterized by reduced rapid eye movement (REM) sleep, increased slow-wave sleep (N3), and a high prevalence of sleep-related breathing disorders such as obstructive sleep apnea—affecting up to 79% of this population (Chawla & Heussler, 2018; Lal et al., 2015). These disturbances contribute to sleep fragmentation, reduced daytime alertness, and impaired cognitive functioning.

Recent studies have reported that children with DS exhibit reduced spindle density, delayed interhemispheric synchrony, and atypical topographical distribution of sleep spindles (Shetty et al., 2023). These findings resemble those described in other neurodevelopmental conditions, supporting the hypothesis that sleep spindles could serve as useful markers for clinical monitoring and early intervention in this vulnerable group (Gruber & Wise, 2016; Kwon et al., 2023).

This study aims to quantitatively and topographically characterize sleep spindles in children with Down syndrome through retrospective analysis of their polysomnographic recordings. The analysis includes spindle density, spatial distribution, interhemispheric symmetry, and temporal synchrony, seeking to identify distinctive patterns that could enhance our understanding of neurophysiological development in this population. The approach aligns with current clinical guidelines recommending sleep studies in children with DS for early detection of sleep-related disorders.

METHODS

Participants

This cross-sectional observational study, with a retrospective design, was conducted through the review of polysomnographic records of children with Down syndrome, aged between 3 and 18 years. The recordings were collected between 2017 and 2023 at the Pediatric Sleep Center of the Pontificia Universidad Católica de Chile. A convenience sampling strategy was used, resulting in a total of 13 analyzable cases, limited by technical constraints and the impact of the COVID-19 pandemic.

Participants were selected based on the quality of their polysomnographic recordings, ensuring that basic oscillatory patterns during sleep stages were not disrupted by motor artifacts. Eleven channels of interest were analyzed, distributed across the frontal, central, parietal, occipital, and frontopolar regions—five in the left hemisphere, five in the right, and one reference channel.

This study received approval from the institutional ethics committee, and written informed consent was obtained from the parents or legal guardians of all included participants [ID: 230608007, 08/03/2023].

Polysomnography

In this study, the Respironics Alice 5 polysomnography system (PSG) was used to assess the sleep patterns of the participants. This device allows for detailed monitoring of multiple physiological channels, such as brain (EEG), ocular (EOG), activity (EMG), and cardiac activity (ECG). The system setup included 11 electroencephalographic channels Filtered with a high-pass filter of 0.32 Hz and a low-pass filter of 47.6 Hz. All EEG channels had a sampling rate of 100 samples per second. Additionally, muscle activity in the chin and ocular activity were recorded. See Table 1, for channel information details.

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

Table 1

Channel names for polysomnographic recordings

Hemisphere	Region	Channel
Left	Frontopolar	P1-A2
Left	Frontal	F3-A2
Left	Central	C3-A2
Left	Parietal	P3-A2
Right	Frontopolar	P2-A1
Right	Central	C4-A1
Right	Parietal	P4-A1
Right	Occipital	O1-A2
Right	Occipital	02-A1
Left	Electrooculogram	EOG
Right	Electrooculogram	EOG
	Muscle Activity	EMG

Hypnogram

Alice 5 software allows for the automated creation of hypnograms, identifying the different stages of the sleep-wake cycle in participants. However, for this research, a classification was performed through visual inspection, following the guidelines established by the American Academy of Sleep Medicine (version 3) to evaluate the sleep microarchitecture of each participant. This was crucial for classifying the sleep stages into N1, N2, and N3.

Spectral Analysis

To visually characterize the temporal evolution of spectral power and assess the stability of sleep-wake transitions across the night, multitaper spectrograms were computed following the methodology described by Babadi and Brown (2014). EEG recordings were divided into 30-second epochs, each extended by 15 seconds at both ends to reduce edge-related spectral distortions. This yielded an effective analysis window of 60 seconds per epoch.

For each extended segment, the signal was centered by subtracting the mean and analyzed using discrete prolate spheroidal sequences (DPSS) as tapers. The number of tapers was adjusted dynamically based on a target spectral resolution of 0.5 Hz. Power spectral density (PSD) estimates were computed across the frequency range of 0.5–30 Hz by averaging the squared magnitudes of the FFTs from all tapers.

Spectral power values were log-transformed (log10) and intensity-saturated at the 2.5th and 97.5th percentiles to enhance visual contrast. These spectrograms were used descriptively to monitor the spectral continuity of each channel, verify signal quality, and qualitatively track transitions between vigilance states. Epochs were later aligned with the hypnogram to enable visual segmentation of individual sleep stages for further representation.

To further describe the frequency content of each sleep-wake cycle state, we computed average power spectra across sleep stages using state-resolved aggregation of the multitaper spectrograms. Each spectrogram was structured as a time-by-frequency matrix, with rows representing consecutive 30-second epochs and columns corresponding to spectral bins from 0.5 to 30 Hz. Epochs were previously classified according to manually scored hypnograms as wakefulness (DES), N1, N2, N3, or REM sleep. For each sleep stage, all corresponding epochs were

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

selected and their power values averaged along the time dimension, yielding a mean spectral profile per state and channel. Log-transformed power values were used for improved contrast and interpretability.

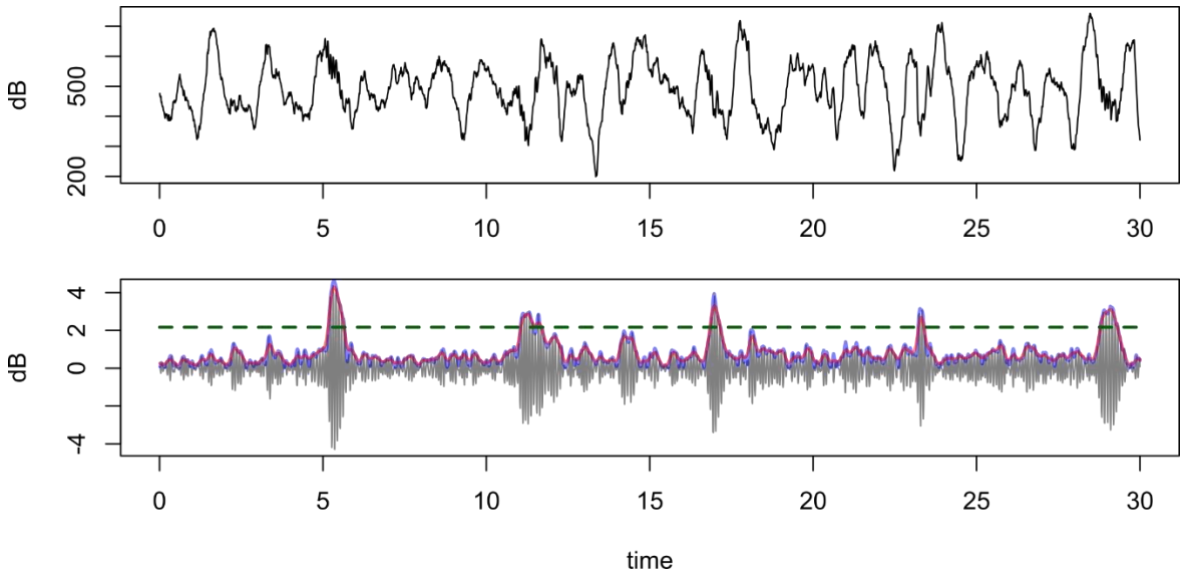
These averaged spectra were then overlaid using semi-transparent color coding to visually compare the frequency profiles of different states. This visualization allowed us to characterize the spectral features associated with each state of the sleep-wake cycle and to verify consistency with hypnogram-based scoring.

Sleep Spindle Detection

After artifact removal and participant selection, an algorithm for sleep spindle detection was applied, based on Martin et al. (2012) and Nir et al. (2011). First, a second-order Butterworth filter was applied around 10 and 15 Hz (Rangayyan & Krishnan, 2015). This was performed for the entire recording period, and to avoid edge effects, a copy of the signal of interest was added at each end. Once the filtering was completed, the total recording time was selected, excluding the edges. Next, the Hilbert transform was applied to estimate the signal envelope, which was used as a reference point for calculating the sleep spindle density. The Hilbert transform provides the instantaneous amplitude of the filtered signal. The entire signal was divided into 30-second epochs, corresponding to those identified in the hypnogram of each participant. Only those epochs identified as N2 were selected, and the 90th percentile (P90) value was calculated to determine a cutoff point for the amplitude of the recorded signal. Figure 1 illustrates the effect of signal filtering on the identification of sleep spindles.

Figure 1

Filtering procedure to sleep spindle exploration



Note. The upper panel showcases the polysomnography signal of a 30-second channel sample in its raw state, while in the lower panel, the Filtered signal from 10 to 16 Hz is shown. The red horizontal line represents a threshold created to estimate the presence or absence of a sleep spindle. In this context, there would be 5 sleep spindles in this epoch.

Since the recording had a sampling rate of 100 points per second, only those values whose amplitude exceeded P90 and had a duration of at least 50 points, that is, half a second, were considered as sleep spindles, considering the temporal distribution of the sleep spindle. A filter from 10 to 15 Hz was applied to each channel.

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

Symmetry and Synchronization calculation

To evaluate the symmetry of sleep spindles, pairs of channels were compared topographically, that is, those with the same location but in different hemispheres. The Pearson correlation coefficient was used to determine whether the temporal distribution of the number of sleep spindles was symmetric between the hemispheres. Moreover, cross-correlation was applied to estimate whether the occurrence of sleep spindles coincided with the previous or subsequent epochs, allowing for a detailed assessment of interhemispheric synchrony.

Topoplots

The 11 channels included in the polysomnogram were used as references to describe the sleep spindle density topographically. The Matlab software with the eeglab package was used to illustrate the density of sleep spindles in each participant, as well as the global density obtained. This procedure was carried out for the 10 to 16 Hz range for a general characterization of sleep spindles, and then the 10 to 13 Hz and 14 to 16 Hz ranges were selected to characterize slow and fast sleep spindles, as described in the literature. The topoplot was used to describe the greatest density of relative sleep spindles in comparison with different locations. However, these are not absolute values in terms of density. A relative ranking was performed, where the data were ordered from those that described the highest density of sleep spindles to those that described the lowest density of sleep spindles. Under this approach, magnitude of density spindles is lost, since ranking does not consider true magnitude of density.

Data Analysis

The R software was used to analyze data. Non-parametric statistics were applied, considering the sample size, to evaluate differences in the density of sleep spindles across different channels, as well as to compare the density between different frequency ranges. For pairwise comparisons between channels, the *Wilcoxon W* test was used, while Friedman test was implemented to determine significant differences between multiple channels.

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

RESULTS

Population features

Table 2 presents a comprehensive description of the sample utilized, detailing sex, birth weight, the presence of epilepsy, brain lesions, and medication usage.

Table 2

Clinical and individual characteristics of each participant

PSG	Age (years)	Sex	RN (weeks)	Birth weight (grams)	Epilepsy	Medications	Other pathologies	Structural Brain Injury	Weight (kg)	Size (cm)	BMI	
1	14	1	37	2950	2	levothyroxine, sertraline, ezetimibe-simvastatin	1,2	2	43	146	20.2	p64
2	2	1	35	2060	2	levothyroxine, levocetirizine, melatonin, risperidone, clobazam for behavior	1,4,8	2	11.4	83	16.5	p50
3	7	1	36	3000	2	levothyroxine, desloratadine, methylphenidate	1, 5, 6, 7	2	24.5	107	21.4	p97
4	4	2	36	3010	2	None	4	2	17	100	17	p87
5	3	2	38	2875	2	desloratadine, fluticasone nasal	4	2	14	90	17.3	p87
6	6	1	38	3900	2	desloratadine, montelukast, mometasone nasal, risperidone, methylphenidate	4,6,7,8	2	25	112	19.9	p96.8
7	6	2	38	3035	2	Levothyroxine	1	2	33.5	121	22.9	p99
8	7	2	37	3320	2	methylphenidate, vitamin D	3,6	2	18.5	112	14.7	p32
9	3	1	35	2280	2	Melatonin	7	2	12	90	14.8	p13
10	1	2	26	730	1	levetiracetam, levothyroxine, desloratadine	1,4,9	2	10.2	75		p60
11	6	2	38	2835	2	montelukast, fluticasone nasal, rupatadine	4, 7	2	28.5	120	19.8	p96
12	13	1	37	2690	2	Levothyroxine	1,7	2	45	146	21.1	p80
13	0 (3 months)	1	38	3460	2	levocetirizine, fluticasone buccal, iron	2,7,10	2	5.5	62		p80

Note. Sex is recorded as 1 for male and 2 for female. Additionally, the presence of epilepsy is denoted by (1) and the absence by (2). No brain lesions were observed in any participant. The presence of other pathologies is as follows: 1. Hypothyroidism, 2. Congenital heart disease, 3. Celiac disease, 4. Allergic rhinitis, 5. Bronchial asthma, 6. Attention deficit and hyperactivity disorder, 7. Obstructive sleep apnea, 8. Behavioral disorder, 9. Epilepsy, 10. Transient secondary hypoventilation.

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

Sleep Architecture

Through the analysis of polysomnography, the different stages of the sleep-wake cycle were identified. Table 3 summarizes the identification of the various stages for the 13 participants in the study.

Table 3
Sleep stages for all 13 participants.

PSG	Age	N1%	N2%	N3%	REM%
1	14	4.7	53.7	21.4	20.2
2	2	3.0	45.7	39.5	11.8
3	7	2.5	51.4	30.2	15.9
4	4	2.3	53.1	30.6	13.9
5	3	1.9	35.8	46.5	15.8
6	6	7.7	47.4	23.7	21.2
7	6	2.0	30.9	46.2	21
8	7	2.2	66.9	25.5	3.4
9	3	0	57.2	37.1	5.7
10	1	3.1	54.8	32.9	9.3
11	6	1.9	39.7	39.7	18.7
12	13	0.3	69.3	15.9	14.5
13	0 (3 months)	7.7	41	38.4	12.9

Note. N1, N2 and N3, respectively refers to the percentage of non-rem sleep stages.

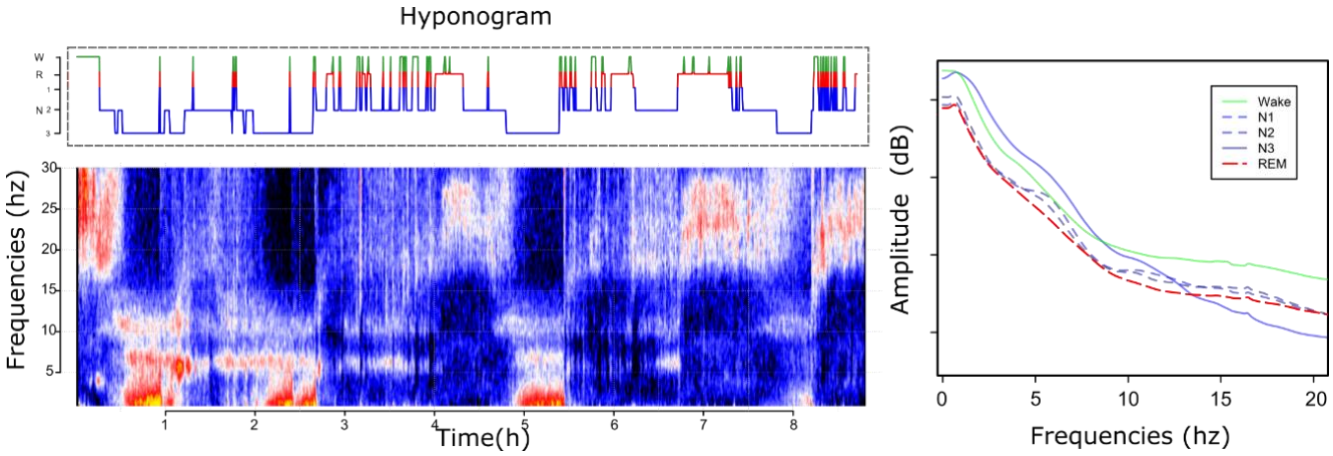
Reference values were used to assess the differences in the densities of the stages of the sleep-wake cycle. It was identified that subjects diagnosed with Down syndrome had an average of 32.89% (*SD* = 9.5) of N3 sleep during the recording night. With 95% confidence, it is estimated that the true population value lies between 27.18% and 38.6% of N3 sleep. This value indicates that the time spent in N3 is not compatible with the reference values for N3 in healthy individuals (15% to 25% of N3). Additionally, a reduction in REM sleep was observed compared to healthy subjects (20% to 25%), with the sample averaging 14.1% (*SD* = 5.6) of REM sleep. With 95% confidence, it is estimated that the true value lies between 10.8% and 17.6% of REM sleep during the night, making it incompatible with the expected values in healthy subjects.

Time-frequency analysis of the electroencephalographic activity of the participants reveals that the main features of the sleep-wake cycle are preserved. Figure 2 presents the hypnogram of a representative subject, accompanied by a time-frequency chart. It can be observed that the subject's spectrum clearly differentiates the stages of the sleep-wake cycle. During the non-REM sleep phases, an increase in delta band activity is noted, while the periods identified as N2 and N3 show oscillations around 10 Hz. It is worth mentioning that during these stages, oscillations around 5 Hz are also observed, which coincides with the periods of sleep in its second and third stages. Additionally, Figure 2 (right panel) illustrates the decline of the spectrogram under different sleep-wake cycle conditions. It is noticeable that during N2 and N3, oscillations around both 10 Hz and 5 Hz appear, with the latter coinciding with the former in the spectrogram.

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

Figure 2

Spectral characterization of the different sleep stages



Note. The upper panel shows a hypnogram, with the frequency spectrum to the right. In green, wakefulness is indicated; in red, REM sleep; and in blue, non-REM sleep. The central panel displays a time-frequency chart, consistent with the hypnogram, to identify oscillatory activity at different frequencies. The right panel shows the average power spectral density for each sleep stage (Wake, N1, N2, N3, REM), allowing comparison of frequency distribution across states."

Sleep Spindles density

A sleep spindle count was performed using three different Filters (10-15 Hz, 10-13 Hz for slow spindles, and 14-15 Hz for fast spindles). When reducing the bandwidth, a higher spindle density was identified, with the highest density observed in the fast spindle band. The largest differences were seen in the occipital and central channels, showing an increase in density when applying the narrower Filter. When comparing the spindle density between fast spindles (14-15 Hz) and slow spindles (10-13 Hz), it was found that the fast band shows a higher density. This finding suggests that fast spindles may be a characteristic phenomenon of N2 sleep in children with Down syndrome. It was observed that, on average, the channels described approximately one spindle per epoch. Figure 3 illustrates the behavior of the average spindle density across the three Filter types.

A higher spindle density was observed in the parietal, occipital, and central regions. Most of the spindles were found in the left and posterior channels when evaluating the 10-16 Hz band. For slow spindles (10-13 Hz), a lateralization to the left and posterior regions was also observed, while fast spindles (14-16 Hz) lateralized to the anterior channels. Statistical tests, such as the Wilcoxon test, showed significant differences in spindle density between the C3 and C4 channels for slow spindles (*Wilcoxon statistics* = 74, $p < 0.05$). However, this was significant only when considering the channels filtered for slow sleep spindles. For other channel pairs, such as F3-F4 and Fp1-Fp2, no significant differences were found ($p > 0.05$) in any of the other conditions.

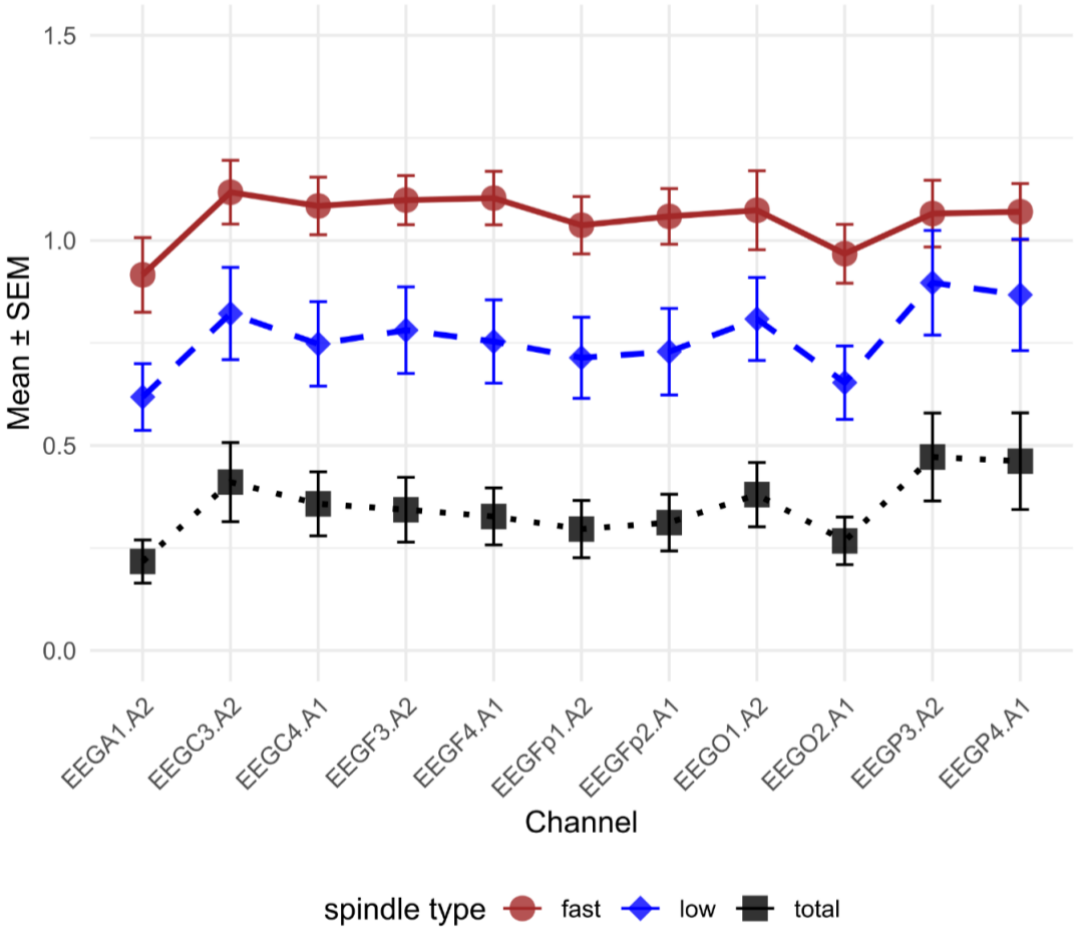
A two-factor analysis of variance (ANOVA) was conducted to assess the effect of the variables "Channel" and "Filter" on the dependent variable. The analysis revealed that the "Channel" variable had a significant effect on the dependent variable, with an F value of 1.857 and a p-value of 0.0497, indicating that at least one channel differs significantly from the others. On the other hand, the "Filter" variable showed a highly significant effect, with an F value of 174.025 and a p-value less than 0.0001, suggesting clear differences between the different conditions. However, the interaction between "Channel" and "Filter" was not significant, with an *F* value of 0.144 and a p-value of 1.0000, indicating that the effect of one variable does not depend on the level of the other.

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

Finally, it was observed that the model residuals showed a sum of squares of 40.75, suggesting that there is variability not explained by the model.

Figure 3

Density of spindles as function of channel and filter



Note. Describes the density of sleep spindles for each described condition.

Symmetry and Synchrony

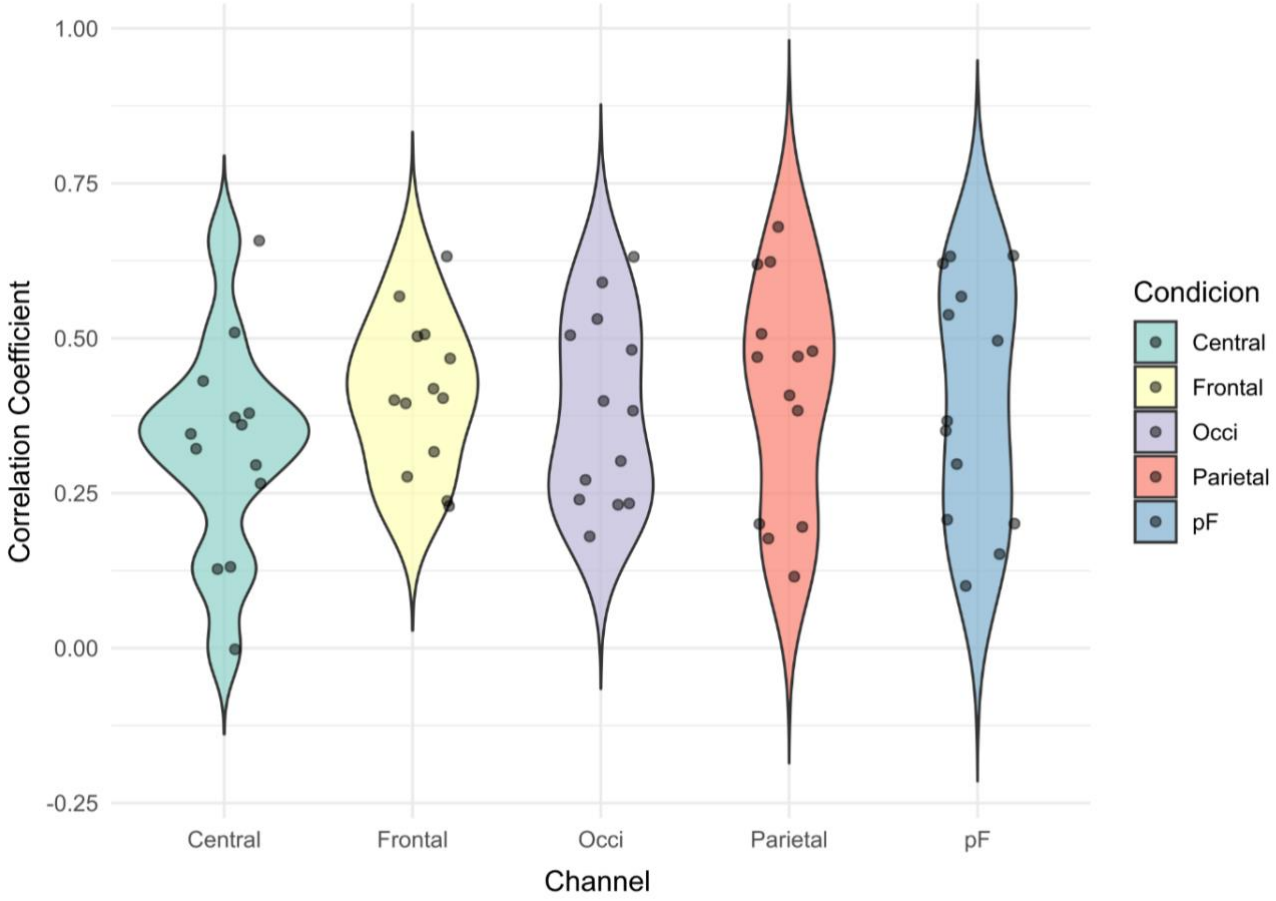
Symmetry was evaluated based on the Pearson correlation coefficient. The time series of sleep spindles detected for each epoch were taken, and then a correlation was performed with the equivalent channel from the other cerebral hemisphere. An average was extracted across all subjects, and the goal was to determine whether there were any differences in spindle density between the hemispheres. The analysis of variance (ANOVA) indicated that the "Channel" factor did not have a significant effect on the measurements ($F(4, 60) = 0.623$, $p = 0.648$). This suggests that there are no statistically significant differences between the channels. The Friedman test revealed that there were no significant differences in the measurements between the channels (*Friedman chi-square* = 5.2923, $df = 4$, $p = 0.2586$). This suggests that there is insufficient evidence to differentiate the asymmetry of the channels.

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

Despite this, it is important to highlight that among the different channels, the correlation coefficient reached a maximum average correlation coefficient of 0.4, with a standard deviation of 0.12. This suggests that, in general, symmetry is observed when considering the timing of the occurrence of sleep spindles. However, since there is no established standard for comparison, it is difficult to definitively determine the level of symmetry between hemispheres. See Figure 4.

Figure 4

Correlation Coefficient for spindles per epoch through two hemispheres



Note. average per subject of the correlation coefficient between channels of each hemisphere is shown. Each violin plot represents a channel pair at a specific location. Central, Frontal, Occi, Parietal and pF, refers to electrode location.

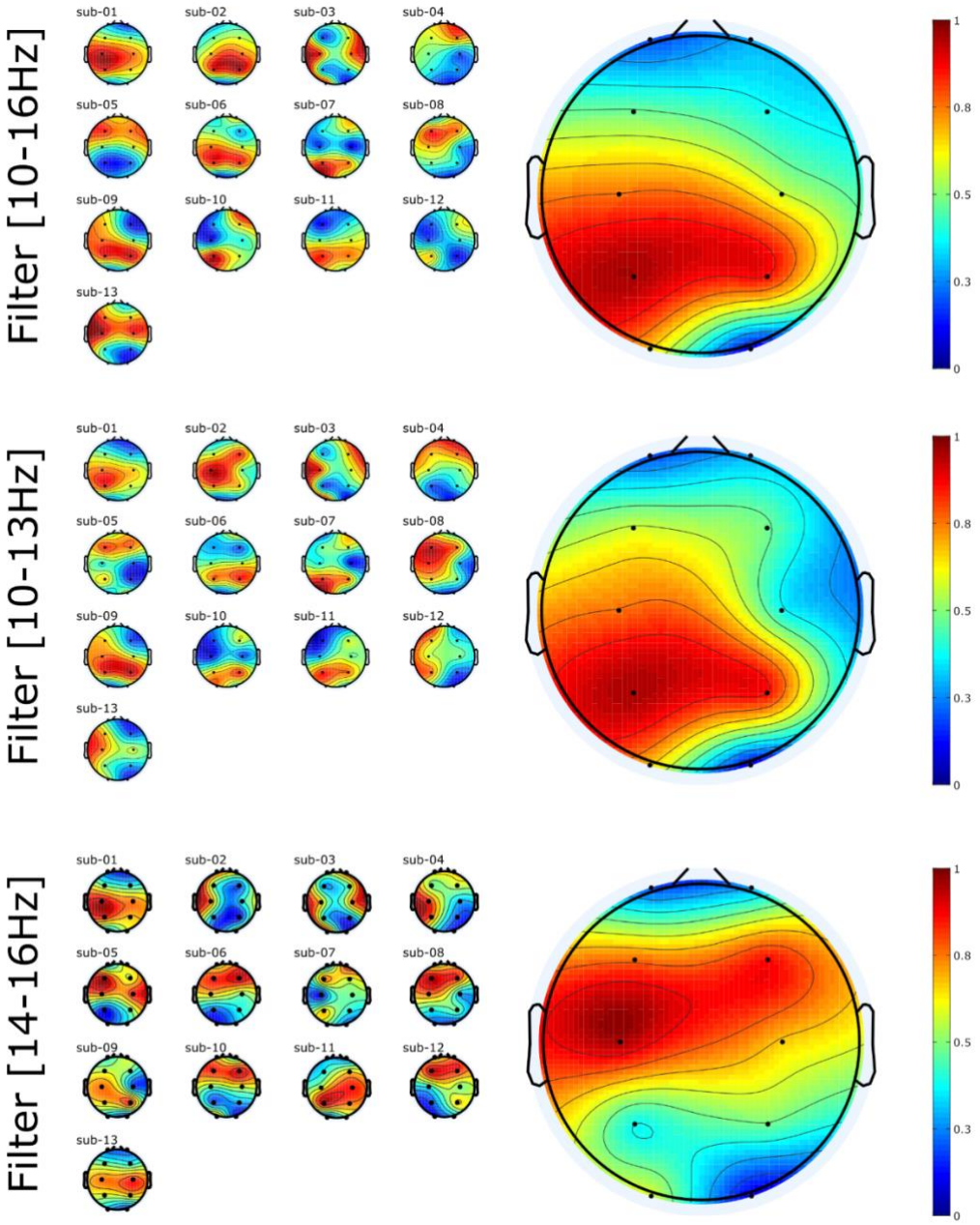
Topographic Distribution of Sleep Spindles

The topographic characterization of spindle density in the 10 to 16 Hz range (Figure 5, top) reveals a predominant distribution towards the left hemisphere, especially in the posterior channels. This same leftward lateralization is also observed in the distribution of spindle density between 10 and 13 Hz (Figure 5, middle), with spindles being primarily located in the posterior regions. However, when analyzing higher frequency spindles, specifically in the 14 to 16 Hz range (Figure 5, bottom), a shift in topographic distribution is noted, with a greater concentration in the anterior channels, though left lateralization remains a prominent feature.

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

Figure 5

Topographic characterization of spindle density



Note. Top, spindle density between 10 to 16 Hz, Middle, spindle density 10 to 13 hz. Bottom, spindle density between 14 to 16hz.

DISCUSSION

The results of this study highlight key alterations in the architecture and microstructure of sleep in Down syndrome (DS) children, which may be linked to both genetic and anatomical factors, with significant implications for cognition. Here we discuss the main results, their possible explanations, and future directions for more comprehensive research.

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

Sleep architecture alterations

One of the most relevant findings of this study was the reduction in REM sleep and the increase in slow-wave sleep (N3) in children with Down syndrome (DS). This phenomenon has been previously described in studies such as those by Nisbet (2014) and is associated with a reorganization of synaptic balance during sleep. The synaptic homeostasis hypothesis proposed by Tononi and Cirelli (2006) suggests that this increase in slow waves could be a compensatory response to the energy demands of wakefulness, particularly in the face of the cortical imbalance observed in children with DS (Geiger et al., 2024). This imbalance, characterized by an increase in theta power and a decrease in alpha power, reflects an abnormal interaction between the mechanisms of cortical excitation and inhibition.

Alterations in Sleep Spindles

Another notable Sinding is the reduction in sleep spindle density, particularly slow spindles, which are linked to explicit memory. In studies such as those by Dehnavi et al. (2023), it was observed that the integration between slow spindles and slow sleep oscillations is crucial for the consolidation of explicit memories. Talukder et al. (2023) conducted an analysis of the oscillatory components in individuals with Down syndrome (DS) and controls, showing a significant reduction in the sigma band, where sleep spindles occur, while delta activity remained relatively intact. This finding suggests a reorganization of brain oscillations during sleep in children with DS, which could be key to understanding how alterations in sleep spindles affect memory consolidation.

Possible explanations

Genetic Factors

Studies in animal models such as Ts65Dn and Ts1Cje have identified the triplication of genes like SOD1 and APP, which are implicated in sleep and electroencephalogram alterations (Colas et al., 2008; Zhang et al., 2023). These genes may contribute to the emergence of altered sleep phenotypes, such as reductions in REM sleep or alterations in theta oscillations during NREM sleep. However, the conclusions drawn from these animal models are limited due to species differences, with their extrapolation being more evident in relation to sleep disorders.

For example, Ts65Dn mice show an increase in theta frequency during NREM sleep and a delay in sleep rebound after sleep deprivation, reflecting alterations in sleep homeostatic mechanisms. While these observations are helpful for understanding the molecular effects of genetic triplication, they do not necessarily represent the behavioral and cognitive manifestations observed in humans.

Anatomic Factors

The anatomical characteristics of Down syndrome (DS) have a significant impact on sleep quality. Alterations such as mandibular hypoplasia, macroglossia, hypotonia, and enlarged tonsils contribute to a reduction in the size of the upper airways, increasing the risk of obstructive sleep apnea (OSA) (Lal et al., 2015). Additionally, the frequent presence of obesity in this population exacerbates airway collapse during sleep (Chawla & Heussler, 2018).

These conditions are also associated with frequent awakenings and sleep fragmentation, which reduces the amount of REM sleep and directly affects memory consolidation (Sibarani et al., 2022). Research has also highlighted that the typical craniofacial dysmorphology of DS could influence the distribution of sleep spindles, affecting their synchrony and topography. For example, studies by Gombos et al. (2022) identified that the frontal regions show alterations in the amplitude and frequency of spindles, which could partially explain the characteristic cognitive decline.

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

Finally, the altered topographic distribution of sleep spindles in children with Down syndrome (DS) may be linked to a delay in cortical maturation. This phenomenon has been observed in studies analyzing the relationship between spindles and anatomical development (Shetty et al., 2023), highlighting the need for a comprehensive approach to understand how these structural differences affect sleep functionality.

Spindle, environmental demand and synaptic homeostasis

The interaction between environmental demands and synaptic homeostasis mechanisms may be key to understanding the alterations observed in sleep spindles in Down syndrome (DS) children. The synaptic homeostasis hypothesis (Tononi & Cirelli, 2006) proposes that sleep, particularly slow-wave sleep and spindles, plays a crucial role in restoring synaptic efficacy after daily activity. In the case of children with DS, environmental demands, such as higher social and educational expectations, could intensify synaptic deterioration, creating a greater need for neuronal consolidation during sleep.

Kumral (2023) and Martin (2013) highlighted that a reduction in spindle density, particularly in frontal regions, is associated with deterioration in cognitive functions such as learning and memory. These findings allow the interpretation that the reduction in slow spindles in children with Down syndrome (DS) could contribute to the alterations observed in explicit memory, exacerbated by an environment that does not always adapt to their needs.

Additionally, Talukder et al. (2023) described those anomalous oscillations, such as the reduction in sigma activity combined with the preservation of delta activity, could be indicative of a compensatory attempt by the brain to maintain synaptic plasticity. This imbalance could be related to an inability to efficiently generate sleep spindles, limiting the ability of sleep to fulfill restorative functions. Therefore, the combination of intense environmental demands and inherently altered sleep could accelerate cognitive deterioration in this population.

Future directions

It is essential to explore phenomena such as the Cyclic Alternating Pattern (CAP) (Parrino et al., 2012) and the build-up of slow-wave sleep (Achermann & Borbély, 1990) to better understand the underlying mechanisms in children with Down syndrome (DS). These patterns could provide new indicators of sleep quality and efficiency (Gombos et al., 2022). On the other hand, by qualitatively reviewing the brain activity of the participants, it was possible to identify a theta band oscillation during N2. This oscillation is not typically observed in the spectrogram of a typical individual during non-REM sleep. On the contrary, the theta band typically shows high amplitude during wakefulness. No evidence of this pattern was found in similar literature (e.g., Talukder et al., 2023), so it is worth asking whether it could be a unique marker for the sample studied. Finally, it is important to consider a comprehensive evaluation of symptomatology to identify co-morbid factors that may be negatively impacting sleep quality in patients, factors not solely determined by genetic alterations. Being able to identify these alterations, and above all, educate about the relevance of sleep, could have a significant impact on both the quality of life of individuals with DS and promote resources to cope with the cognitive demands of daily life.

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

CONCLUSIONS

This study provides a detailed characterization of sleep spindle dynamics in children with Down syndrome, revealing altered density, topographic distribution, and moderate interhemispheric synchrony. The observed increase in slow-wave sleep and reduction in REM sleep aligns with prior descriptions of disrupted sleep architecture in this population. Moreover, the predominance of spindle activity in left and posterior regions may reflect atypical cortical organization or delayed neurodevelopment — a hypothesis that warrants further investigation. While the clinical applicability of spindle measures remains to be established, these findings suggest that sleep spindle analysis could serve as a potential neurophysiological marker in future diagnostic or monitoring approaches for children with Down syndrome.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data is not publicly available due to privacy or ethical restrictions.

FUNDINGS:
This research did not receive specific funding from public, commercial, or not-for-profit agencies.

CONFLICT OF INTEREST:
All authors declare no conflict of interest.

Author Contributions(CRediT):

Conceptualization: María Olga Retamal Rosales, J. Amaro-Fuenzalida, Tomás Mesa Latorre
Methodology: J. Amaro-Fuenzalida
Data Curation: J. Amaro-Fuenzalida, Juan Pablo Retamal Rosales
Formal Analysis: Juan Pablo Retamal Rosales
Investigation: María Olga Retamal Rosales, Jovita Corzo Lameiro
Resources: Tomás Mesa Latorre, Tomás Ossandón Valdés
Writing – Original Draft: María Olga Retamal Rosales
Writing – Review & Editing: J. Amaro-Fuenzalida, Tomás Ossandón Valdés
Supervision: Tomás Mesa Latorre, Gregorio Sierra Del Villar
Visualization: J. Amaro-Fuenzalida

Todos los autores han leído y aceptado la versión publicada del manuscrito

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

REFERENCES

Achermann, P., & Borbély, A. A. (1990). Simulation of Human Sleep: Ultradian Dynamics of Electroencephalographic Slow-Wave Activity. *Journal Of Biological Rhythms*, *5*(2), 141-157. https://doi.org/10.1177/074873049000500206

American Academy of Sleep Medicine. (2007). *The AASM manual for the scoring of sleep and associated events: Rules, terminology and technical specifications*. Westchester, IL: American Academy of Sleep Medicine.

Au, C. H., & Harvey, C. (2020). Systematic review: the relationship between sleep spindle activity with cognitive functions, positive and negative symptoms in psychosis. *Sleep Medicine X*, *2*, 100025. https://doi.org/10.1016/j.sleepx.2020.100025

Babadi, B., & Brown, E. N. (2014). A Review of Multitaper Spectral Analysis. *IEEE Transactions On Biomedical Engineering*, *61*(5), 1555-1564. https://doi.org/10.1109/tbme.2014.2311996

Chatburn, A., Coussens, S., Lushington, K., Kennedy, D., Baumert, M., & Kohler, M. (2013). Sleep Spindle Activity and Cognitive Performance in Healthy Children. *SLEEP*, *36*(2), 237-243. https://doi.org/10.5665/sleep.2380

Chawla, J., & Heussler, H. (2018). Sleep in Down Syndrome. En *InTech eBooks*. https://doi.org/10.5772/intechopen.71065

Colas, D., Valletta, J. S., Takimoto-Kimura, R., Nishino, S., Fujiki, N., Mobley, W. C., & Mignot, E. (2007). Sleep and EEG features in genetic models of Down syndrome. *Neurobiology Of Disease*, *30*(1), 1-7. https://doi.org/10.1016/j.nbd.2007.07.014

Dehnavi, F., Koo-Poeggel, P. C., Ghorbani, M., & Marshall, L. (2023). Memory ability and retention performance relate differentially to sleep depth and spindle type. *iScience*, *26*(11), 108154. https://doi.org/10.1016/j.isci.2023.108154

Geiger, M., Hurewitz, S. R., Pawlowski, K., Baumer, N. T., & Wilkinson, C. L. (2024). Alterations in aperiodic and periodic EEG activity in young children with Down syndrome. *Neurobiology Of Disease*, *200*, 106643. https://doi.org/10.1016/j.nbd.2024.106643

Gombos, F., Bódizs, R., Pótári, A., Bocskai, G., Berencsi, A., Szakács, H., & Kovács, I. (2022). Topographical relocation of adolescent sleep spindles reveals a new maturational pattern in the human brain. *Scientific Reports*, *12*(1). https://doi.org/10.1038/s41598-022-11098-8

Gruber, R., & Wise, M. S. (2016). Sleep Spindle Characteristics in Children with Neurodevelopmental Disorders and Their Relation to Cognition. *Neural Plasticity*, *2016*, 1-27. https://doi.org/10.1155/2016/4724792

Kumral, D., Matzerath, A., Leonhart, R., & Schönauer, M. (2022). Spindle-dependent memory consolidation in healthy adults: A meta-analysis. *bioRxiv (Cold Spring Harbor Laboratory)*. https://doi.org/10.1101/2022.07.18.500433

Kwon, H., Walsh, K. G., Berja, E. D., Manoach, D. S., Eden, U. T., Kramer, M. A., & Chu, C. J. (2023). Sleep spindles in the healthy brain from birth through 18 years. *SLEEP*, *46*(4). https://doi.org/10.1093/sleep/zsad017

Lal, C., White, D. R., Joseph, J. E., Van Bakergem, K., & LaRosa, A. (2015). Sleep-Disordered Breathing in Down Syndrome. *CHEST Journal*, *147*(2), 570-579. https://doi.org/10.1378/chest.14-0266

Martin, N., Lafortune, M., Godbout, J., Barakat, M., Robillard, R., Poirier, G., Bastien, C., & Carrier, J. (2012). Topography of age-related changes in sleep spindles. *Neurobiology Of Aging*, *34*(2), 468-476. https://doi.org/10.1016/j.neurobiolaging.2012.05.020

Nir, Y., Staba, R. J., Andrillon, T., Vyazovskiy, V. V., Cirelli, C., Fried, I., & Tononi, G. (2011). Regional Slow Waves and Spindles in Human Sleep. *Neuron*, *70*(1), 153-169. https://doi.org/10.1016/j.neuron.2011.02.043

Nisbet, L. C., Phillips, N. N., Hoban, T. F., & O'Brien, L. M. (2014). Characterization of a sleep architectural phenotype in children with Down syndrome. *Sleep And Breathing*, *19*(3), 1065-1071. https://doi.org/10.1007/s11325-014-1094-6

Parrino, L., Ferri, R., Bruni, O., & Terzano, M. G. (2011). Cyclic alternating pattern (CAP): The marker of sleep instability. *Sleep Medicine Reviews*, *16*(1), 27-45. https://doi.org/10.1016/j.smrv.2011.02.003

Rangayyan, R. M., & Krishnan, S. (2024). *Biomedical signal analysis*. John Wiley & Sons.

Shetty, M., Davey, M. J., Nixon, G. M., Walter, L. M., & Horne, R. S. C. (2023). Sleep spindles are reduced in children with Down syndrome and sleep-disordered breathing. *Pediatric Research*, *96*(2), 457-470. https://doi.org/10.1038/s41390-023-02854-1

Sibarani, C. R., Walter, L. M., Davey, M. J., Nixon, G. M., & Horne, R. S. C. (2021). Sleep-disordered breathing and sleep macro- and micro-architecture in children with Down syndrome. *Pediatric Research*, *91*(5), 1248-1256. https://doi.org/10.1038/s41390-021-01642-z

Sommer, C., & Henrique-Silva, F. (2008). Trisomy 21 and Down syndrome: a short review. *Brazilian Journal Of Biology*, *68*(2), 447-452. https://doi.org/10.1590/s1519-69842008000200031

Talukder, A., Yeung, D., Li, Y., Anandanadarajah, N., Umbach, D. M., Fan, Z., & Li, L. (2024). Comparison of power spectra from overnight electroencephalography between patients with Down syndrome and matched control subjects. *Journal Of Sleep Research*, *33*(5). https://doi.org/10.1111/jsr.14187

Tononi, G., & Cirelli, C. (2005). Sleep function and synaptic homeostasis. *Sleep Medicine Reviews*, *10*(1), 49-62. https://doi.org/10.1016/j.smrv.2005.05.002

ISSN: 0718-4123
DOI: 10.7714/CNPS/20.2.210

Ulrich, D. (2016). Sleep Spindles as Facilitators of Memory Formation and Learning. *Neural Plasticity*, *2016*, 1-7. https://doi.org/10.1155/2016/1796715

Zhang, Y., Ye, S., Hou, X., Yu, W., Wang, X., Mu, Q., Han, F., & Guo, J. (2023). Possible genetic cross-talk between Down syndrome and obstructive sleep apnea revealed by transcriptomic analysis. *Sleep And Breathing*, *27*(6), 2469-2478. https://doi.org/10.1007/s11325-023-02845-w

Zhu, L., & Zee, P. C. (2012). Circadian rhythm Sleep Disorders. *Neurologic Clinics*, *30*(4), 1167-1191. https://doi.org/10.1016/j.ncl.2012.08.011