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ORIGINAL RESEARCH

Impaired Attention in Children with Obstructive Sleep Apnea: A Preliminary Study of Behavior Combined with Neuroelectrophysiology

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Objective: To investigate how attention is affected in children with obstructive sleep apnea (OSA) using the attention network test (ANT) combined with event-related potential (ERP) and time-frequency analysis.

Methods: Eighty-seven children aged 6–11 years with symptoms of snoring or mouth breathing during sleep were recruited from the Sleep Center of Beijing Children's Hospital from May to July, 2023. All participants completed the Mini-mental State Examination and Attention Deficit Hyperactivity Disorder rating scale. We acquired 32-lead electroencephalography (EEG) data while participants performed the ANT, followed by Polysomnography.

Results: Of the 87 children, 21 had no OSA, 49 had mild OSA, and 17 had moderate to severe (MS) OSA. Each group had similar questionnaire scores, similar response time and accuracy for the different ANT conditions. There are alterations in the processing of three separate components of the attentional network in children with OSA. The amplitude of the N3 component at the F_Z electrode in the MS OSA group was lower than that of the non-OSA and mild OSA groups (all $P<0.05$). In the executi control network phase, the energy of alpha band was higher in the MS OSA group than in the mild OSA group ($Z=-2.624$, $P=0.026$). The mean amplitude of the N3 component at the F_Z electrode was correlated with the obstructive apnea-hypopnea index (OAHI) ($r=0.232$, $P=0.038$).

Conclusion: Attention impairment was observed as a reduced N3 in the frontal area in the MS OSA group, which was correlated with the OAHI. However, questionnaire and behavioral performance did not differ significantly between groups. These findings suggest that the N3 amplitude is a sensitive neuroelectrophysiological marker of OSA-related cognitive impairment.

Keywords: OSA, child, attention, event-related potential, time-frequency

Introduction

Obstructive sleep apnea (OSA) is a sleep disorder of increasing concern in children. It is characterized by the recurrent collapse of the upper airway during sleep, which results in intermittent hypoxemia and sleep fragmentation.[1] This sleep disorder is also associated with a variety of cognitive dysfunctions, such as attention deficits, executive dysfunction, abnormal behavior, and memory impairment,[1–4] which adversely affect the long-term growth and development of children. Our previous study confirmed the damage of OSA to children's attentional networks.[5] However, OSA also has a higher incidence of co-morbidity with atypical attention deficit hyperactivity disorder (ADHD), and ADHD itself is a possible factor in attentional functioning in OSA. The attention network is a core component of cognitive function. To date, few studies have examined this network and the underlying mechanisms in pediatric patients with OSA. The combined analysis of behavioral test and neuroelectric measures,

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such as event-related potential (ERP) and time-frequency (TF) analysis can facilitate our understanding of the neural mechanisms underlying specific cognitive task performance.[6]

Attention is a complex construct that involves multiple functionally and anatomically distinct, yet interactive, networks that enable alerting, orienting, and executive (or conflict) control functions.[5,7] The alerting network, which includes the right frontal and parietal cortices and thalamus, is associated with alertness and vigilance and ensures sensitivity to incoming stimuli and response readiness. The orienting network, which includes the parietal cortex and frontal eye fields, allows the selection of information via the disengagement, shifting, and re-engagement of attention in visual space. The executive control network is also known as the conflict network owing to its involvement in self-regulation and conflict resolution of thoughts, emotions, and overt responses. Regions involved include the anterior cingulate and lateral ventral prefrontal cortices.[8,9] The functioning of these three distinct networks can be examined behaviorally using the attention network test (ANT).[8,10]

ERPs are brain-evoked potentials that reflect the electrophysiological response of the brain to a specific event (eg, a sensory, cognitive, or motor event). By analyzing different ERP components (eg, P1, N1, P2, N2, and P3), we can understand the neural dynamics of information processing.[11–13] TF analysis is used to examine neurophysiological activity by analyzing signal characteristics at different times and frequencies. The energy of signals at different times and frequencies varies depending on the number of synchronously firing neurons and the precision of synchrony and reflects the neural processes that are activated in response to specific cognitive demands.[6,14] Previous ERP studies using the ANT paradigm have demonstrated that cue-stimuli-related P1 and N1 components are associated with alerting and orienting network, whereas target-stimuli-related P3 components are related to the executive control network.[15,16] Therefore, in our study, we considered the P1 and P3 components as important neurophysiological markers.

The aim of the present study was to investigate how attention networks are affected in children with OSA using a children's version of the ANT combined with ERP and TF analysis.

Participants and Methods

Participants

Children were recruited from the Sleep Centre of Beijing Children's Hospital from May 1–July 31, 2023. The inclusion criteria were: 1) children aged 6–11 years; 2) those with symptoms of snoring or mouth breathing during sleep. Exclusion criteria were: those with 1) craniofacial abnormalities, such as Down's syndrome or Crouzon syndrome; 2) genetic metabolic disorders; 3) intellectual disability (ie Mini-mental State Examination [MMSE] score ≤ 17); 4) a history of neurological or psychiatric illness or other pathological condition that could potentially influence the study results. The study was approved by the Ethics Committee of Beijing Children's Hospital. Written informed consent and assent were obtained from the parents or children (for those aged > 8 years).

MMSE

The MMSE is a widely used tool designed to quickly assess an individual's cognitive functioning. The test encompasses seven cognitive domains: orientation in time, orientation in space, memory registration, recall, attention, calculation, and language. We excluded children who scored ≤ 17, corrected for educational level.[17]

Attention Deficit Hyperactivity Disorder (ADHD) Rating Scale

The ADHD rating scale consists of 18 items. Nine items relate to attention-deficit symptoms and nine items relate to hyperactivity and impulsivity symptoms. One point is awarded for each 'yes' response, with higher scores indicating more severe symptoms.[18]

Child Version of the ANT

We used the international version of the ANT.[10] The test was administered by trained staff between 2 pm and 5 pm, before polysomnography (PSG) data acquisition. The E-Prime 2.0 software (Psychology Software Tools, Sharpsburg, PA, USA) was used to program and administer the ANT. The task included four cue types (ie, no cue, central cue, double cue, and spatial cue)

and three target conditions (ie, neutral, congruent, and incongruent). Children were asked to press the left or right mouse button when the central fish was pointing left or right. The paradigm comprised 24 practice sessions and 144 formal sessions, totaling approximately 25 minutes. The ANT and parent interview administrators and the PSG scorers were blind to each other's results. Reaction time (RT) and accuracy rate were recorded for the different cue types and target conditions. The efficiency of the three networks was determined as follows: alerting network = $RT_{no\ cue} - RT_{double\ cue}$, where a larger difference indicates better performance of the alerting network; orienting network = $RT_{central\ cue} - RT_{spatial\ cue}$, where a larger difference indicates better orienting ability; and executive control network = $RT_{incongruent} - RT_{congruent}$, where a larger difference indicates poorer executive control network function. The experimental materials and procedure are shown in Figure 1.

PSG

A standard overnight PSG was performed using the E-series system (Compumedics, Melbourne, Australia) and the Alice 5 system (Respironics, Murrysville, PA, USA). Children were monitored for at least 7 hours. PSG included electroencephalography (EEG); C3/M2, C4/M1, O1/M2, and O2/M1), electrooculography, electromyography, electrocardiography, airflow monitoring (using a nasal cannula and thermistor), and assessments of chest and abdominal respiratory movement, oxygen saturation, snoring, and body position. Sleep stages and respiratory events were scored manually according to the American Academy of Sleep Medicine manual.[19] The obstructive sleep apnea-hypopnea index (OAHI) is the number of episodes per hour of obstructive apnea, mixed apnea, and obstructive hypopnea. An OAHI score of $1 < OAHI \leq 5$ events/hour (e/h), $5 < OAHI \leq 10$ e/h, and > 10 e/h were categorized as mild, moderate, and severe OSA, respectively.[1]

EEG Acquisition and Data Processing

EEG was recorded while participants completed the ANT using the Grael EEG system (Compumedics, Melbourne, Australia) and a 32-channel saline EEG cap. Electrode placement on the EEG cap followed the international 10–20 system. The impedance of all electrodes was kept below 30 kΩ. The EEG was digitized at 2048 hz with a 0.1–100 hz band pass, including a 60-Hz notch filter, and stored for offline averaging. The data were then analyzed offline and re-referenced to averaged whole-brain electrodes in epochs of 1000 ms, which included a 200 ms pre-stimulus period for baseline correction. Epochs exceeding an amplitude of ±100 μV, identified via visual inspection, were rejected as artifacts. The ERP components analyzed were

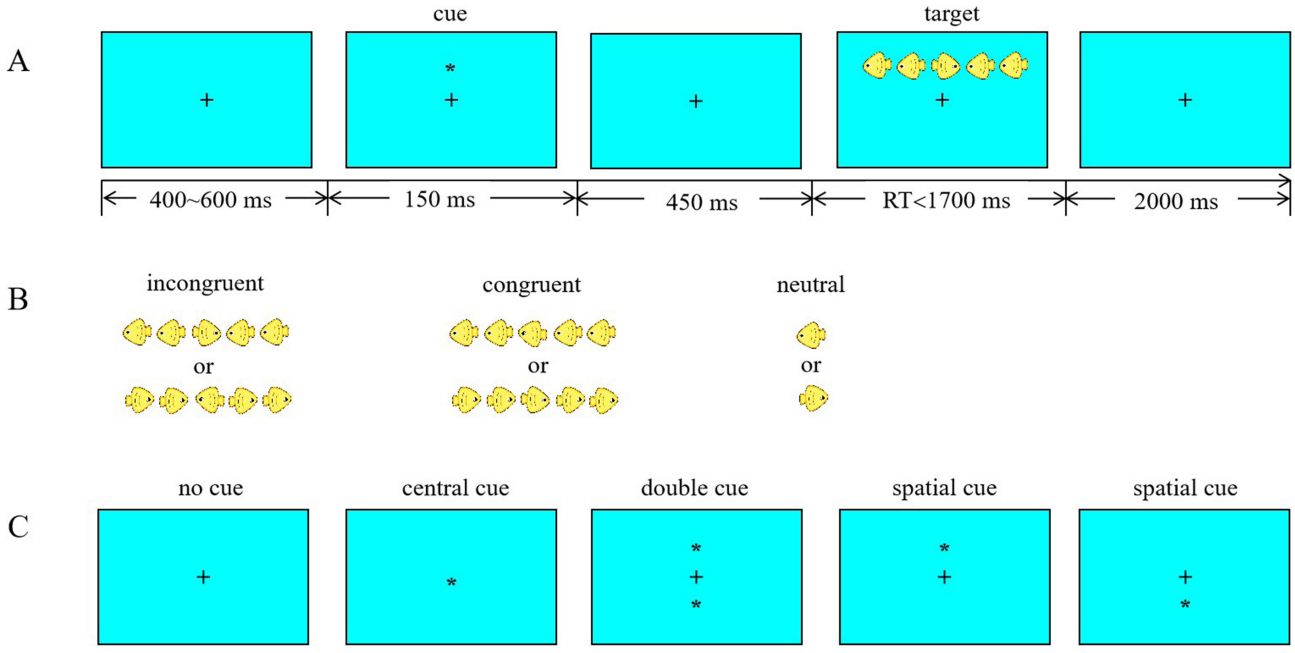

Figure 1 Materials and procedure of the ANT *: cue. (**A**) The sequence of events of the ANT. (**B**) The three target conditions. (**C**) The four cue types.
Abbreviations: RT, reaction time; ms, millisecond.

P1 (100–200 ms), N2 (200–300 ms), and P3 (250–400 ms) of the posterior electrodes (ie, P_3, P_4, P_Z, O_1, O_2, and O_Z) and N1 (100–200 ms), P2 (150–275 ms), and N3 (300–500 ms) of the anterior electrodes (ie, F_Z, F_{CZ}, and C_Z).

The time window used for the TF analysis was −200–1000 ms, and we selected the continuous wavelet transform analysis method. Baseline correction of the energy values was −200–−100 ms, and there was no difference in the energy values of the spectral analysis baseline after the baseline correction. Energy values were extracted for the following frequency bands: delta (1–4 hz), theta (4–7 hz), alpha (8–13 hz), beta (13–30 hz), low beta (13–16 hz), high beta (16–30 hz, and gamma (30–45 hz). These frequency bands were chosen because each captures the distinct neural oscillatory activity associated with specific cognitive processes.

Statistical Analysis

We used the SPSS 26.0 software (IBM Corp., Armonk, NY, USA) for statistical analysis. Normally distributed data are expressed as means ± standard deviations, and data with a skewed distribution are expressed as medians and interquartile ranges (P_{25}, P_{75}). For normally distributed data, groups were compared using an analysis of variance (ANOVA). Subsequent pairwise comparisons to explore between-group differences were conducted using Bonferroni or Tamhane's T2 procedures according to the homogeneity of variances significance. For non-normally distributed data, we used non-parametric tests to evaluate group differences. For comparisons of numerical data, we used the chi-squared test. Correlations between EEG parameters and PSG and clinical parameters were analyzed using partial correlation to correct for age, sex, and body mass index. All tests were two-sided and $P < 0.05$ was considered statistically significant.

Results

A total of 109 children aged 6–11 years who underwent PSG at the sleep center from May 1, 2023, to July 31, 2023, were recruited. One patient had a history of epilepsy, 1 patient had a history of febrile seizures, 1 patient had a history of ADHD, 3 patients had unsuccessful data acquisition, 1 patient had a history of osteomyelitis, and 15 patients were excluded because of poor EEG data quality. This resulted in 87 children who were included in the analysis. A data collection flowchart is shown in Figure 2.

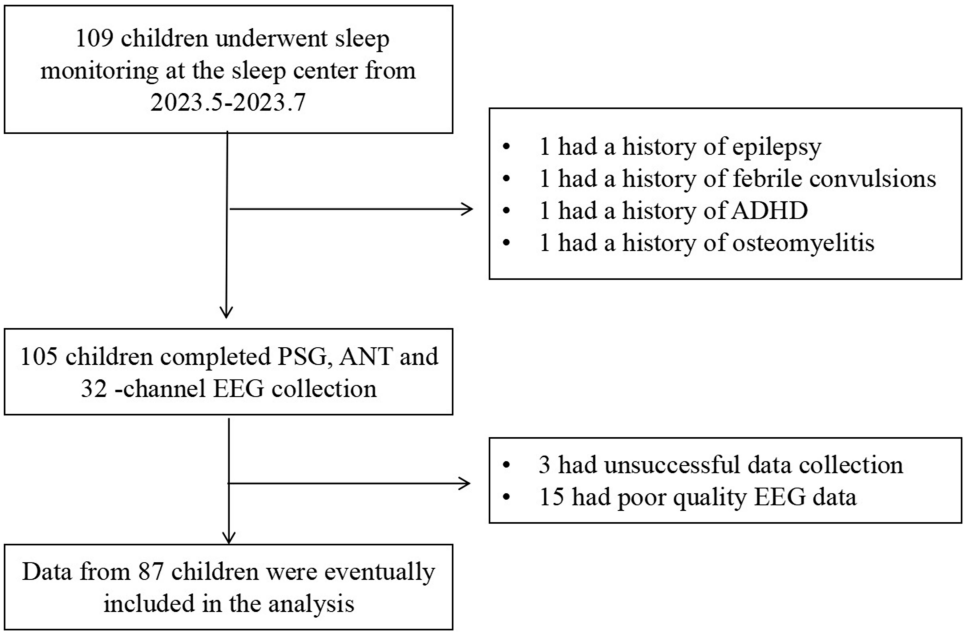

Figure 2 Flowchart of data collection.

Demographic Characteristics and Questionnaire Scores

The demographic characteristics and questionnaire scores of the included children are shown in Table 1. There were 21 children without OSA, 49 with mild OSA, and 17 with moderate to severe (MS) OSA. The body mass index of the MS OSA group was higher than that of the non-OSA group ($P < 0.01$). Age, sex, years of education, MMSE score, and ADHD scale scores did not differ significantly between the three groups.

PSG results

The PSG data of the three groups of children are shown in Table 2. Results showed expected differences, which signified a higher number of respiratory events, more disturbed sleep architecture, and poorer blood oxygenation in the MS OSA group than in the non-OSA and mild OSA groups.

Table 1 Demographic Characteristics and Questionnaire Scores of All Children

	Non-OSA n=21	Mild OSA n=49	MS OSA n=17	Z/F/χ^2	*P*
Age, years	7.8±1.2	7.7±1.2	7.7±1.3	0.088	0.916
Male, n (%)	11(52.3%)	28(57.1%)	15(88.2%)	6.286	0.043
BMI, kg/m^2	15.5(14.2,16.6)	16.9(14.7,20.2)	19.8(16.7,26.2)**	11.865	0.003
Average education years, y	1(0,3)	1(0,2)	1(0,2)	0.321	0.852
MMSE, score	26(23.5,28)	26(22,27.5)	24(20,27.5)	1.432	0.489
ADHD scale					
Attention deficit, score	0.76±0.39	0.97±0.50	0.75±0.35	2.338	0.103
Hyperactivity -impulsive, score	0.63±0.31	0.78±0.49	0.85±0.65	1.058	0.352

Notes: **P<0.01, compared with the non-OSA group.
Abbreviations: OSA, obstructive sleep apnea; MS OSA, moderate to severe OSA; BMI, body mass index; MMSE, Mini-mental State Examination; ADHD, Attention Deficit Hyperactivity Disorder.

Table 2 Comparison of Polysomnographic Results for All Children

	Non-OSA n=21	Mild OSA n=49	MS OSA n=17	Z/F	*P*
TST, min	474.3±59.5	467.0±45.3	421.0±45.5**##	6.761	0.002
SE,%	90.9±5.9	90.3±6.4	83.2±5.5**##	9.717	<0.001
N1%,%	7.4±3.4	9.6±3.7*	15.8±5.1**##	23.017	<0.001
N2%,%	44.0±6.5	44.4±6.2	41.0±3.6	2.263	0.110
N3%,%	25.3±6.8	23.9±6.0	23.6±4.7	0.537	0.586
R%,%	23.3±4.2	22.0±3.7	19.6±4.3**#	4.181	0.019
OAHI, e/h	0.5(0.2,0.7)	2.0(1.5,3.3)**	12.4(6.8,23.4)**##	68.836	<0.001
CAI, e/h	0.4(0.2,1.1)	0.6(0.3,1.6)	0.9(0.3,2.0)	3.068	0.216
ODI, e/h	0.3(0,1.0)	1.3(0.3,2.3)*	8.5 (1.5,14.5)**##	24.094	<0.001
ArI, e/h	6.5(4.5,8.3)	8.0(6.2,9.4)	12.6(11.1,16.0)**##	27.751	<0.001
ArI-resp, e/h	0.4(0.3,0.7)	1.6(1.2,2.8)**	6.8(4.4,10.7)**##	46.603	<0.001
Mean SpO_2, %	98(98,98)	98(97.5,98)	98(96.5,98)	5.945	0.051
Nadir SpO_2, %	94(92,95)	93(91,95)	89(83,90.5)**##	19.238	<0.001
T90, %	0(0,0)	0(0,0)	0(0,0.2)**##	30.761	<0.001

Notes: **P < 0.01, *P < 0.05, compared with the non-OSA group. ##P < 0.01, #P < 0.05, compared with the mild OSA group.
Abbreviations: OSA, obstructive sleep apnea; MS OSA, moderate to severe OSA; TST, total sleep time; SE, sleep efficiency; N1%, N2%, N3%, and R%, percentage of non-REM sleep stage 1, 2, and 3 and REM sleep stage of total sleep time, respectively; OAHI, obstructive apnea-hypopnea index; CAI, central apnea index; ODI, oxygen desaturation index; ArI, arousal index; ArI-resp, respiratory event-related arousal index; SpO_2, peripheral oxygen saturation; T90, proportion of total sleep time with oxygen saturation < 90%; e/h, events/hour.

Table 3 Comparisons of the Attention Network Test Results for All Children

	Non-OSA n=21	Mild OSA n=49	MS OSA n=17	F	*P*
Incongruent RT, s	957.6±118.0	916.7±103.1	903.4±109.5	1.374	0.259
Incongruent ACC, %	93.8±5.4	92.4±8.3	89.9±11.3	0.944	0.393
Congruent RT, s	844.4±127.6	820.6±116.0	831.5±116.9	0.295	0.745
Congruent ACC, %	95.6±4.0	95.4±7.3	95.8±4.8	0.025	0.976
Executive control network efficiency, s	113.2±77.0	96.0±90.2	71.9±82.3	0.971	0.383
No cue RT, s	894.3±132.1	865.3±97.2	863.6±70.2	0.633	0.534
No cue ACC, %	94.1±5.9	92.3±8.9	90.6±10.5	0.713	0.493
Double cue RT,s	837.6±101.3	822.7±101.5	852.1±131.2	0.456	0.636
Double cue ACC, %	94.7±6.6	94.2±6.3	94.2±5.8	0.045	0.956
Alerting network efficiency, s	56.7±85.2	42.6±86.3	11.5±98.4	1.125	0.330
Center cue RT, s	975.9±159.9	945.0±142.2	966.0±164.4	0.341	0.712
Center cue ACC, %	95.4±3.8	95.4±7.2	93.4±9.2	0.497	0.610
Spatial cue RT, s	837.1±129.3	810.5±23.1	796.9±109.3	0.526	0.593
Spatial cue ACC, %	96. 0±4.8	95. 6±7.5	95. 9±6.3	0.033	0.968
Orienting network efficiency, s	138.8±79.6	134.5±110.4	169.1±104.5	0.625	0.538

Abbreviations: OSA, obstructive sleep apnea; MS OSA, moderate to severe OSA; RT, Reaction time; ACC, accuracy.

ANT Results

The ANT data of the three groups of children are presented in Table 3. There were no significant differences between the three groups for response time or accuracy in any of the conditions. There were no significant group differences in the efficiency of the three attention networks (ie, the alerting, orienting, and executive control networks).

ERP Results

There were no significant group differences in the mean amplitude or latency of the P1 component for the P_3, P_Z, P_4, O_1, O_Z, and O_2 electrodes in the alerting network (Supplementary Table 1). The mean amplitude and latency of the P1 component at P_3, P_Z, P_4, O_1, and O_Z electrodes in the orienting network were not significantly different among the three groups. However, the latency of the P1 component at the O_2 electrode was shorter in the mild OSA group than in the non-OSA group (Z=2.630, *P*=0.026; Figure 3 and Supplementary Table 2).

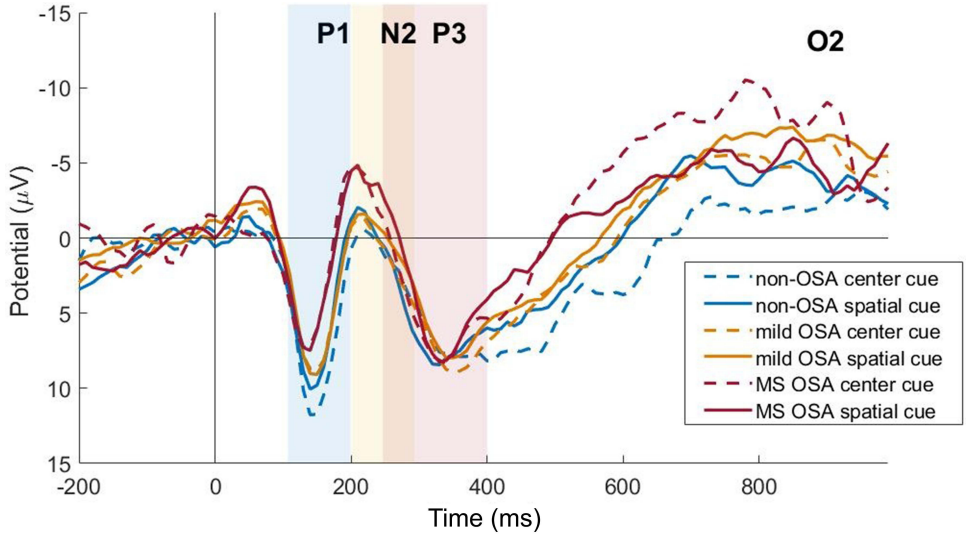

Figure 3 Event-related potential plots of the spatial and central cue types for the three groups.
Abbreviations: MS OSA, moderate to severe OSA; OSA, obstructive sleep apnea.

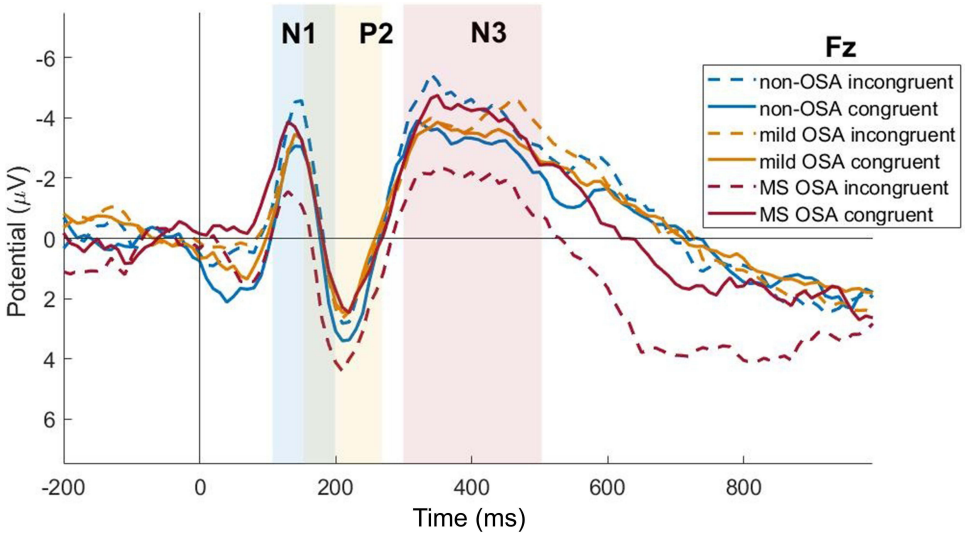

Figure 4 Event-related potential plots of the incongruent and congruent target conditions for the three groups.
Abbreviations: MS, moderate to severe; OSA, obstructive sleep apnea.

For the executive control network, the mean amplitude of the N3 component at the F_Z electrode in the MS OSA group was lower than that of the non-OSA and mild OSA groups (MS OSA group vs non-OSA group, Z=−2.905, *P*=0.011; MS OSA group vs mild OSA group, Z=−2.538, *P*=0.033; Figure 4 and Supplementary Table 3). There were no significant differences among the three groups for the other conditions.

TF Analysis Results

For the alerting network phase, the energy of the high-beta band was higher in the mild OSA group than in the non-OSA group at the P_Z electrode (Z=−2.766, *P*=0.017) and in the MS OSA group at the O_2 electrode (Z=3.164, *P*=0.005). There were no significant differences among the three groups for the other conditions (Figure 5A and B and Supplementary Table 4).

There were no significant differences among groups for the energy values in the orienting network phase (Supplementary Table 5).

For the executive control network phase, the energy of the alpha band was higher in the MS OSA group than in the mild OSA group at the P_Z electrode (Z=−2.624, *P*=0.026). There were no other significant differences (Figure 6 and Supplementary Table 6).

Correlation Analysis

The partial correlation results are shown in Table 4. The mean amplitude of the N3 component at the F_Z electrode was significantly correlated with the OAHI (r=0.232, *P*=0.038). The energy of the high-beta band at the O_2 electrode in the alerting network phase was correlated with N2%.

Discussion

We investigated the function of the attention networks in children without OSA and those with mild and MS OSA. Questionnaire and behavioral results were similar across the three groups. However, the neuroelctrophysiological indicators of the OSA groups were significantly different from those of the non-OSA group. Specifically, children with mild OSA were hyper-vigilant, which caused their orienting network to be activated earlier to ensure normality of more advanced cognitive processing. Children with MS OSA had a sleepier brain when performing an executive control task; their cognitive control was impaired, as reflected by their significantly reduced N3 amplitude at the F_Z electrode. In addition, the N3 amplitude at the F_Z electrode correlated with the OAHI, which is an indicator of OSA severity. Our findings suggest that neuroelctrophysiological indicators can help detect OSA-related neurocognitive impairment earlier and more accurately than questionnaires and behavioral tests.

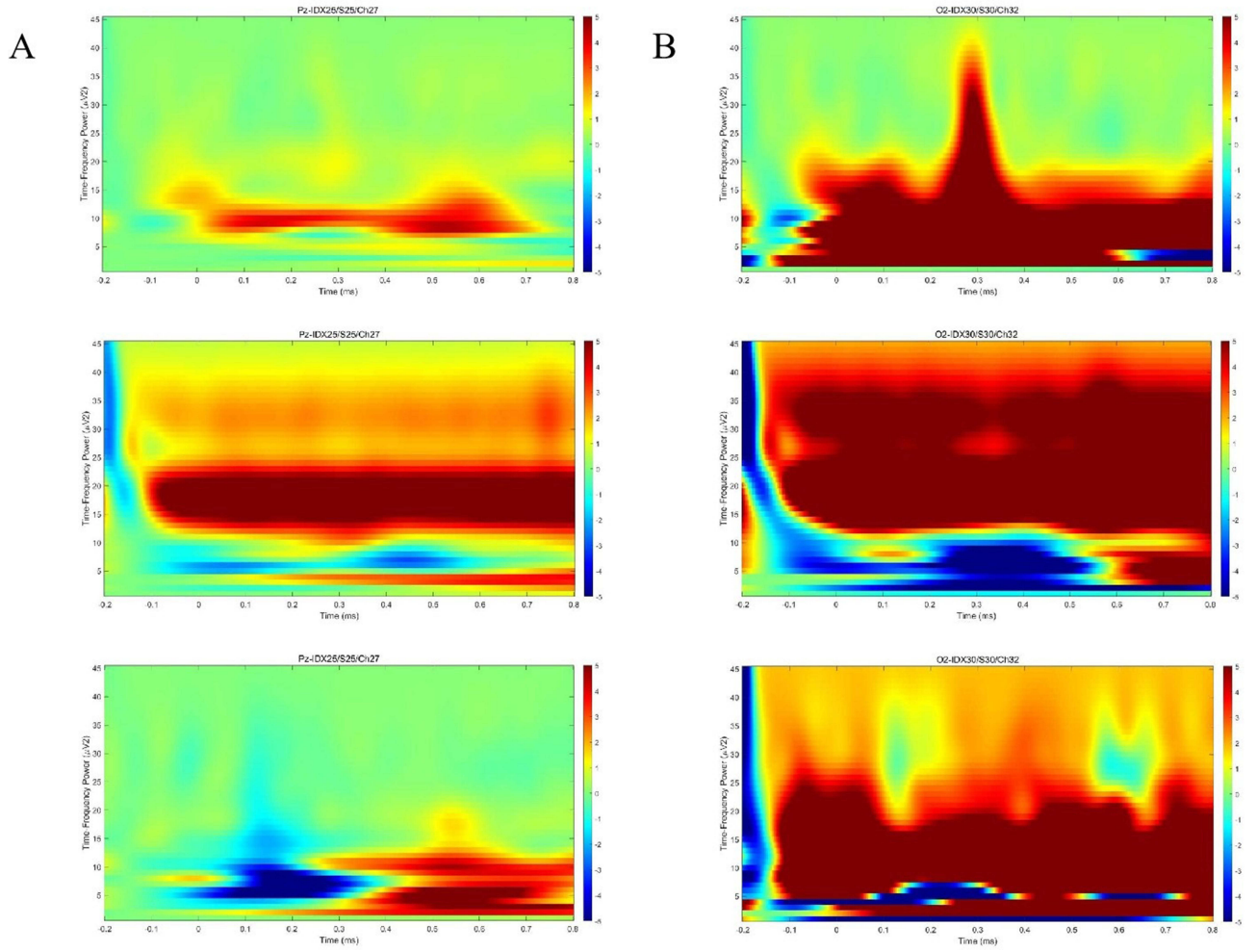

Figure 5 Spectrograms of the P_Z and O_2 electrodes for the alerting network phase. The top panels show the non-obstructive sleep apnea (OSA) group, the middle panels show the mild OSA group, and the bottom panels show the moderate to severe (MS) OSA group. (**A**) The energy of the high-beta band (vertical coordinate at 16–30 hz, horizontal coordinate at 0.1–0.2ms) was higher in the mild OSA group than in the non-OSA group (Z=−2.766, *P*=0.017) at the P_Z electrode. (**B**) The energy of the high-beta band (vertical coordinate at 16–30 hz, horizontal coordinate at 0.1–0.2ms) was higher in the mild OSA group than in the MS OSA group at the O_2 electrode (Z=3.164, *P*=0.005).

Before proceeding to the discussion of medically relevant content, there is a technical issue that needs to be clarified. The ERP waveform in the posterior area is opposite to that in the anterior area because of the averaging of electrodes across the whole brain, which were used as reference electrodes. Therefore, the N3 component of the frontal region electrodes in our study is comparable to the P3 component reported in previous literature.[20]

Alerting and Orienting Networks

Alerting is defined as heightened response preparation in response to external warning stimuli. Orienting refers to the ability to prioritize sensory input by selecting a modality or location and shifting attention (eg, by distracting and refocusing attention).[8] The P1 component, an early component of the attention process, is enhanced with increasing attention load, which reflects the early processing of stimuli.[16,21] In addition, the attended stimulus can evoke a larger N1 amplitude.[21] The amplitudes of the P1 and N1 components reflect a sensory gain control mechanism that leads to perceptual processing of the attended stimulus.[22] ERP studies have shown that P1 and N1 components appear in parietal and occipital regions 80–200 ms after stimulus presentation and are related to alerting and orienting functions of the attention network.[22] Our study showed that children with mild OSA had higher energy in the high-beta band and shorter latency of the P1 component than those with non-OSA. We speculate that when children with mild OSA perform the

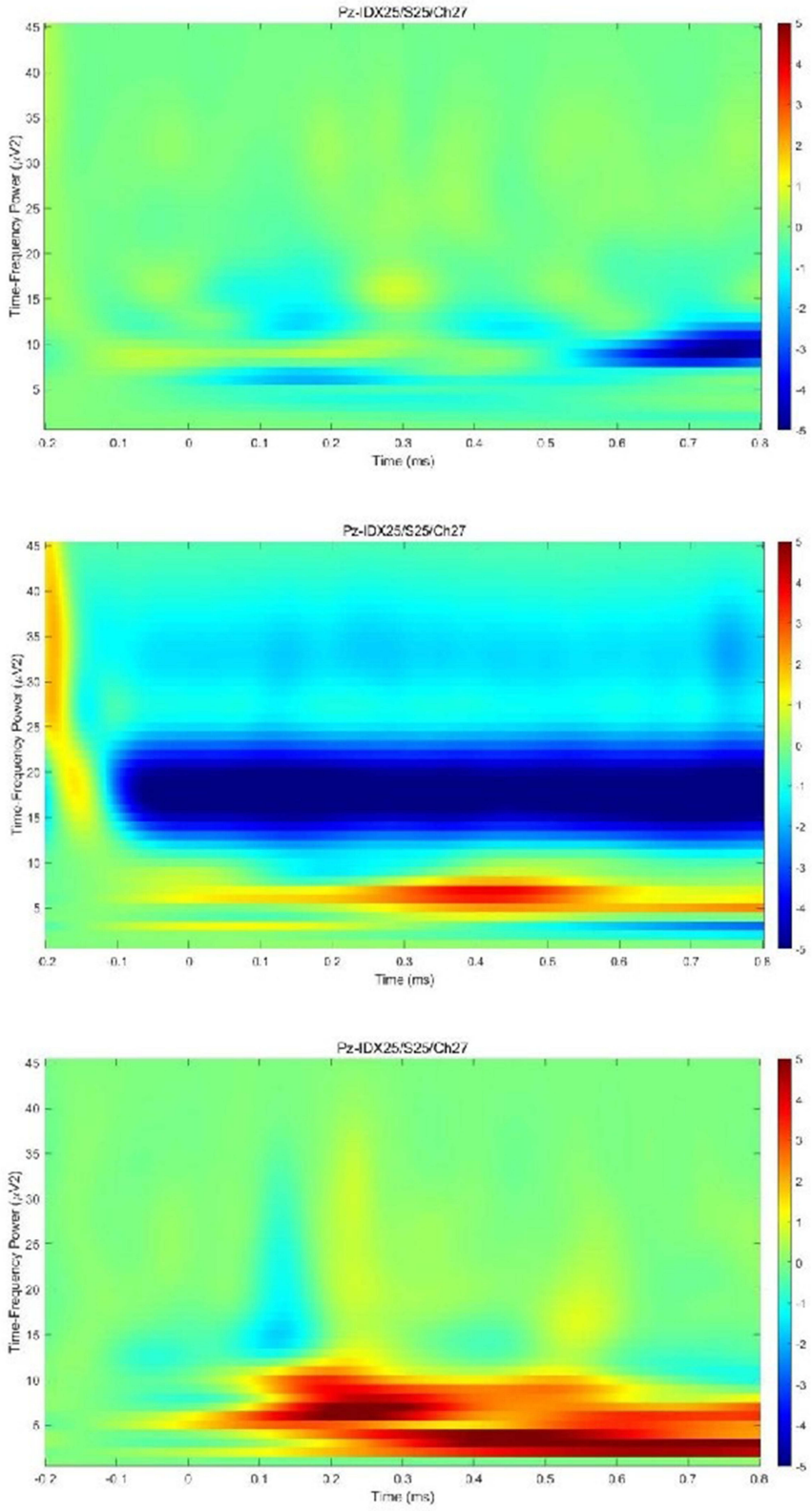

Figure 6 Spectrograms of the P_Z electrode for the executive control network phase. The top panels show the non-obstructive sleep apnea (OSA) group, the middle panels show the mild OSA group, and the bottom panels show the moderate to severe (MS) OSA group. The energy of the alpha band (vertical coordinate at 8–13 hz, horizontal coordinate at 0.25–0.4ms) was higher in the MS OSA group than in the mild OSA group at the P_Z electrode (Z=−2.624, P=0.026).

Table 4 Correlations Between Electrophysiological Parameters and Polysomnographic and Clinical Indicators

	Electrophysiological Parameters				
	lat_P1_DX_O_2	ave_N3_ZX_F_Z	HB_JJ_P_Z	HB_JJ_O_2	A_ZX_P_Z
PSG and clinical indicators					
TST	0.106	−0.103	0.144	0.193	−0.067
N1%	−0.157	0.146	−0.114	−0.15	0.161
N2%	0.099	−0.024	0.173	0.24*	−0.141
N3%	−0.009	−0.072	0.006	−0.027	0.103
REM%	0.047	−0.025	−0.132	−0.139	−0.13
OAHI	0.138	0.232*	−0.039	−0.108	0.066
ODI	0.188	0.179	0.01	−0.058	−0.009
ArI	0.027	0.185	−0.056	−0.092	0.153
ArI-resp	0.062	0.182	−0.047	−0.034	0.07
Mean SpO_2	−0.08	−0.024	−0.131	−0.11	0.138
Nadir SpO_2	−0.043	−0.064	−0.053	0.032	0.03
T90	0.125	0.1	0.003	−0.019	0.074
Attention deficit score	−0.126	0.003	0.191	0.158	0.011
Hyperactivity-impulsive score	−0.09	0.168	0.009	0.017	−0.003
MMSE	0.083	−0.137	0.108	0.15	−0.07
Executive control network efficiency	0.114	−0.004	−0.075	0.028	0.013
Alerting network efficiency	0.023	−0.011	−0.02	0.044	0.085
Orienting network efficiency	0.212	0.059	−0.156	−0.196	0.138

Notes: Correlation analysis controlling for age, sex, and body mass index. *$P < 0.05$.

Abbreviations: lat_P1_DX_O_2, latency of the P1 component at the O_2 electrode in the orienting network; ave_N3_ZX_F_Z, mean amplitude of the N3 component at the F_Z electrode in executive control network; HB_JJ_Pz, energy of the high-beta band at the P_Z electrode for the alerting network phase; HB_JJ_O_2, energy of the high-beta band at the O_2 electrode for the alerting network phase; A_ZX_Pz, energy of the alpha band at the P_Z electrode for the executive control network phase; MMSE, Mini-mental State Examination; PSG, polysomnography; TST, total sleep time; N1%, N2%, N3%, and R%, percentage of non-REM sleep stages 1, 2, and 3 and REM sleep stage of total sleep time, respectively; OAHI, obstructive apnea-hypopnea index; ODI, oxygen desaturation index; ArI, arousal index; ArI-resp, respiratory event-related arousal index; SpO_2, peripheral oxygen saturation; T90, proportion of total sleep time with oxygen saturation < 90%.

ANT task, they are hyper-vigilant approximately 100–200 ms after presentation of the cue stimuli, which results in early activation of the orienting network. Hyper-vigilance may be a compensatory mechanism for OSA-related sleep disturbances that enables children to remain alert during the daytime to cope with the demands of learning and daily activities. Such a compensatory mechanism has been reported in other diseases. One study using resting-state functional MRI showed increased functional connectivity from the thalamus to cuneus, fusiform gyrus, and lingual gyrus in isolated rapid eye movement sleep behavior disorder patients compared with healthy controls, which were thought to reflect a compensatory mechanism for cognitive impairment.[23] We similarly suggest that the mild OSA group possessed such a compensatory mechanism because they exhibited comparable or higher efficiency of the alerting network during the ANT, which may indicate the early stages of OSA-related cognition impairment.

Executive Control Network

The executive control network involves conflict control and resolution during habitual response inhibition, decision-making, and error detection.[8] The P3 component is a latent component commonly used in studies of executive control,[16] and its amplitude and latency reflect the amount of attention resources allocated to external events in the environment and cognitive processing speed, respectively.[24,25] A smaller P3 component indicates a reduction in conflict-resolving ability, where the smaller the amplitude, the fewer attention resources available.[16] Reductions in the P3 component have been reported in patients with ADHD, which suggests that these patients recruit fewer cortical resources during attentionally demanding tasks.[6] In our study, children with MS OSA showed a significantly smaller N3 component than non-OSA and mild OSA children, which indicated that their attentional resources were limited and that they were at risk of resource depletion in the later stages of the task. In addition, we observed that children with MS OSA exhibited higher levels of sleepiness, as indicated by the

higher energy of the alpha band in the executive control network phase. The posterior-occipital alpha band is considered an index of cognitive control and an inverse measure of cortical excitability.[21] Taken together, we speculate that children with MS OSA are in a state of low arousal and are unable to adequately allocate attentional resources when performing an attentionally demanding task. This is consistent with a previous report that demonstrated that intermittent hypoxemia and sleep fragmentation in children with OSA results in daytime tiredness and sleepiness; moreover, this sleepiness is particularly pronounced during cognitively demanding tasks.[26] Furthermore, such cognitive deficits in children with OSA may have long-term effects on academic performance and daily functioning. Therefore, early diagnosis and effective treatment of OSA are crucial for improving the cognitive development of children with OSA.

Neuroelectrophysiological Indicators Have the Potential to Be More Sensitive Than Questionnaire and Behavior Measures

There were no significant differences in the MMSE or ADHD scale scores among the groups. This may have been because the MMSE and ADHD scale are not sufficiently sensitive in detecting cognitive deficits associated with OSA. We found similar results for the ANT behavioral test. However, the neuroelectrophysiological indices were significantly different among groups, and were correlated with the OAHI score. Furthermore, our findings are consistent with our previous large-scale behavioral observations, which showed that children with mild OSA have the most hyperactive alerting network among healthy controls and children with MS OSA.[5] By taking advantage of the high temporal resolution of ERPs, we revealed that mild OSA primarily impacts the early stages of attentional network processes. In this group, this change is still in a compensatory phase; thus, their executive control functions normally. However, MS OSA results in poor executive control, which likely signifies a stage of decompensation of the neurocognitive processes associated with OSA. A longitudinal follow-up study is needed to clarify this hypothesis.

Limitation

This is the first study to evaluate the attention networks of children with varying severity levels of OSA while measuring EEG during the attention task. However, there are several limitations that must be considered in the interpretation of our results. Our study was conducted in a relatively small number of participants and lacked a healthy control group. In addition, because it was a cross-sectional study, the compensatory phase in children with mild OSA and progression from the compensatory phase in MS OSA could not be established. Furthermore, whether the neuroelectrophysiological indicator alterations can be restored by OSA intervention needs to be explored. In addition, it should be noted that a number of factors can influence attention levels, including the educational attainment of the child's parents, the presence of ADHD and the emotional state of the child at the time. Despite our efforts to control for these variables, it is important to acknowledge that they may still have an impact on the results.

Conclusion

This study provided electrophysiological evidence of alterations in the processing of three separate components of the attentional network in children with OSA. The alerting network is hyperactive in children with mild OSA and that the attention and cognition are maintained via a compensatory mechanism. Children with MS OSA showed higher levels of sleepiness during a control task and had difficulty integrating and evaluating stimulus information, which indicated impaired attentional resource allocation and inhibitory control. The neuroelectrophysiological indicators have the potential to be more sensitive than questionnaire and behavior measures to detect OSA-related cognitive impairment.

Declaration of Helsinki

This study complies with the Declaration of Helsinki.

Abbreviations

ADHD, Attention Deficit Hyperactivity Disorder; ANT, attention network test; EEG, electroencephalography; ERP, event-related potential; MMSE, mini-mental State Examination, OAHI, obstructive sleep apnea-hypopnea index; OSA, obstructive sleep apnea; TF, time-frequency.

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An unauthorized version of the Chinese MMSE was used by the study team without permission, however this has now been rectified with PAR.

The MMSE is a copyrighted instrument and may not be used or reproduced in whole or in part, in any form or language, or by any means without written permission of PAR (www.parinc.com).

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Disclosure

The author reports no conflicts of interest in this work.

References

1. Working Group of Chinese Guideline for the Diagnosis and Treatment of Childhood OSA, Subspecialty Group of Pediatrics, Society of Otorhinolaryngology Head and Neck Surgery, Chinese Medical Association, Subspecialty Group of Respiratory Diseases, Society of Pediatrics, Chinese Medical Association, et al. Chinese guideline for the diagnosis and treatment of childhood obstructive sleep apnea (2020)[J]. *Pediatr Investig*. 2021;5(3):167–187. doi:10.1002/ped4.12284
2. Tang Y, Yang C, Wang C, Wu Y, Xu Z, Ni X. Impaired declarative memory consolidation in children with REM sleep-related obstructive sleep apnea. *J Clin Sleep Med*. 2024;20(3):417–425. doi:10.5664/jcsm.10892
3. Marcus CL, Brooks LJ, Draper KA, et al. Diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics*. 2012;130 (3):576–584. doi:10.1542/peds.2012-1671
4. Blechner M, Williamson AA. Consequences of Obstructive Sleep Apnea in Children. *Curr Prob Pediatr Ad*. 2016;46(1):19–26.
5. Wu Y, Wang Y, Wang C, et al. Characteristics of the attentional network in children with sleep-disordered breathing. *Nat Sci Sleep*. 2023;15:719–727. doi:10.2147/NSS.S413330
6. Hasler R, Perroud N, Meziane HB, et al. Attention-related EEG markers in adult ADHD. *Neuropsychologia*. 2016;87:120–133. doi:10.1016/j.neuropsychologia.2016.05.008
7. Posner MI, Petersen SE. The attention system of the human brain. *Annu Rev Neurosci*. 1990;13:25–42. doi:10.1146/annurev.ne.13.030190.000325
8. Fan J, McCandliss BD, Sommer T, Raz A, Posner MI. Testing the efficiency and Independence of attentional networks. *J Cognitive Neurosci*. 2002;14(3):340–347. doi:10.1162/089892902317361886
9. Posner MI, Rothbart MK. Research on attention networks as a model for the integration of psychological science. *Annu Rev Psychol*. 2007;58:1–23. doi:10.1146/annurev.psych.58.110405.085516
10. Rueda MR, Fan J, McCandliss BD, et al. Development of attentional networks in childhood. *Neuropsychologia*. 2004;42(8):1029–1040. doi:10.1016/j.neuropsychologia.2003.12.012
11. Picton TW, Bentin S, Berg P, et al. Guidelines for using human event-related potentials to study cognition: recording standards and publication criteria. *Psychophysiology*. 2000;37(2):127–152. doi:10.1111/1469-8986.3720127
12. Zhang M, Gong X, Jia J, Wang X. Unpleasant odors affect alerting attention in young men: an event-related potential study using the attention network test. *Front Neurosci-Switz*. 2021;15:781997. doi:10.3389/fnins.2021.781997
13. Helfrich RF, Knight RT. Cognitive neurophysiology: event-related potentials. *handb clin neurol*. 2019;160:543–558.
14. Deiber MP, Ibanez V, Missonnier P, Rodriguez C, Giannakopoulos P. Age-associated modulations of cerebral oscillatory patterns related to attention control. *Neuroimage*. 2013;82:531–546. doi:10.1016/j.neuroimage.2013.06.037
15. Neuhaus AH, Urbanek C, Opgen-Rhein C, et al. Event-related potentials associated with attention network test. *Int J Psychophysiol*. 2010;76 (2):72–79. doi:10.1016/j.ijpsycho.2010.02.005
16. An X, Tao G, Zhang X, Ma H, Wang Y. Attention network changes of high-altitude migrants. *Aerosp Med Hum Perf*. 2022;93(11):791–799. doi:10.3357/AMHP.6061.2022
17. Kang JM, Cho YS, Park S, et al. Montreal cognitive assessment reflects cognitive reserve. *Bmc Geriatr*. 2018;18(1):261. doi:10.1186/s12877-018-0951-8
18. Consensus on pediatric clinical practice of early identification, standardized diagnosis and treatment of attention deficit hyperactivity disorder. *Zhonghua Er Ke Za Zhi*. 2020;58(3):188–193. doi:10.3760/cma.j.issn.0578-1310.2020.03.006
19. Berry RB, Quan SF, Abreu AR, et al. *The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. Version 2.6*. Darien, IL: American Academy of Sleep Medicine; 2020.
20. Luck SJ, Kappenman ES. *The Oxford Handbook of Event-Related Potential Components*. Oxford University Press, Oxford;2011
21. Ahumada-Mendez F, Lucero B, Avenanti A, et al. Affective modulation of cognitive control: a systematic review of EEG studies. *Physiol Behav*. 2022;249:113743. doi:10.1016/j.physbeh.2022.113743
22. Zhang D, Zhang X, Ma H, Wang Y, Ma H, Liu M. Competition among the attentional networks due to resource reduction in Tibetan indigenous residents: evidence from event-related potentials. *Sci Rep-UK*. 2018;8(1):610. doi:10.1038/s41598-017-18886-7
23. Byun JI, Kim HW, Kang H, et al. Altered resting-state thalamo-occipital functional connectivity is associated with cognition in isolated rapid eye movement sleep behavior disorder. *Sleep Med*. 2020;69:198–203. doi:10.1016/j.sleep.2020.01.010

24. Hillman CH, Kamijo K, Scudder M. A review of chronic and acute physical activity participation on neuroelectric measures of brain health and cognition during childhood. *Prev Med*. 2011;52 Suppl 1:S21–8. doi:10.1016/j.ypmed.2011.01.024
25. Abramov DM, Pontes M, Pontes AT, et al. Visuospatial information processing load and the ratio between parietal cue and target P3 amplitudes in the attentional network test. *Neurosci Lett*. 2017;647:91–96. doi:10.1016/j.neulet.2017.03.031
26. Beebe DW, Gozal D. Obstructive sleep apnea and the prefrontal cortex: towards a comprehensive model linking nocturnal upper airway obstruction to daytime cognitive and behavioral deficits. *J Sleep Res*. 2002;11(1):1–16. doi:10.1046/j.1365-2869.2002.00289.x