ORIGINAL RESEARCH

Efficient Sleep, Enhanced Attention: Exploring the Interplay With RBC-Inflammation Mechanisms in Hypoxic High-Altitude Areas

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Purpose: The complex interplay between sleep and attention, especially in the suppression of environmental information, is not well understood. This study investigates the bidirectional influence between sleep quality and executive control—an essential aspect of attention—and seeks to uncover the biological pathways involved in this relationship in hypoxic high-altitude areas.

Patients and Methods: We recruited 140 han Chinese juniors from Tibet University, all originally from lowland areas. Participants underwent an attention network test with concurrent electroencephalography to assess attentional function. Sleep quality was evaluated using the Pittsburgh Sleep Quality Index, while the Symptom Check-List-90 and a standard physical examination measured overall health status. A breaking continuous flash suppression task gauged conscious perception breakthrough capacity.

Results: Our findings reveal a bidirectional link between sleep quality and executive control function, which appears to be related to an inflammatory response associated with erythrocyte attributes. Specifically, the P1 and N1 orienting amplitudes mediated the effects of sleep on executive control. This relationship suggests that executive control may, in turn, regulate sleep patterns, with implications for mental health. We also found that enhanced sleep efficiency was correlated with a balance between alerting functions and executive control.

Conclusion: The study establishes that sleep quality and executive control are interlinked via an inflammatory response related to red blood cell characteristics, impacting mental health. Better sleep correlates with improved cognitive performance, suggesting that sleep is crucial for optimal attention resource management and overall cognitive well-being. This enhances our knowledge of the biological foundations of the sleep-attention interaction.

Keywords: plateau sleep, attention, erythrocyte, inflammation

Introduction

Sleep and attention, both engaging in environmental information suppression, are reciprocally influenced and may be impacted by high altitude conditions.[1–3] Studies highlight that high-altitude exposure can disrupt cognitive resource allocation and conflict monitoring, both crucial for attention maintenance and sleep regulation.[4–8] This interplay under hypoxic conditions offers insights into the fundamental nature of sleep and attention.

Attention initiates information processing, bringing and regulating consciousness, and comprises alerting, orienting, and executive control functions.[9–11] Orienting attention selects and suppresses stimuli through alpha oscillations, similar to how sleep uses slow waves to block external inputs, suggesting both employ low-frequency oscillations for information suppression.[12,13] Executive control, key in resolving conflict and bolstered by effective orienting, is essential for working memory.[14,15] Sleep deprivation impairs all three attentional components, while increased daytime attention

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demands enhance sleep drive in typically developing youth but not in those with attention deficit hyperactivity disorder (ADHD).[16–19] The increased attention load in the daytime, such as prolonged cognitive tasks, can also activate the sympathetic nervous system and increase sleep onset latency.[20] These findings imply that there may exist an interaction between sleep and attention. Since executive control is in the highest hierarchy of attention networks and responsible for decision making as well as action,[21] it is worthwhile to delve into whether executive control has a bidirectional relationship with sleep.

High-altitude hypoxia provides a natural model to explore the interplay between sleep and attention networks. This environment reduces human oxygen consumption, eliciting erythrocyte and immune responses reflecting adaptation.[22–25] While increased red blood cells (RBCs) aid oxygen transport, overly high levels can cause chronic mountain sickness (CMS) characterized by sleep issues and oxidative stress, yet its causality with erythrocytosis remains unclear.[26,27] Inflammation promotes survival under sudden hypoxia, but chronic inflammation can lead to cardiovascular complications in conditions like obstructive sleep apnea syndrome (OSAS).[28,29] With mild traumatic brain injuries in military personnel, consciousness loss is associated with heightened inflammation, linking consciousness—and by extension executive control—to inflammatory responses.[30,31] Our previous study already using electroencephalogram and electrocardiogram proved that erythrocytes indirectly influence executive control and the other two attention networks, mediated by inflammatory processes and heart rate variability.[32] Besides high-altitude has also been proved to influence awareness detection, awareness access speed and conscious experiences, together with the executive role of mental imagery.[33–35] And the individual differences of vividness of mental imagery are shaped by alerting network.[36] Erythrocytes can influence immune process. For example, hemoglobin (HGB) generates reactive oxygen species to promote innate immunity function, activates toll-like receptor 4 to promote immune response, or prevents the growth of yeast and bacteria to maintain immune quiescence.[37] One study figured out erythrocytes can also influence white blood cell (WBC) changes that affect executive control via consciousness, impacting mental health.[38] The detrimental effects of inflammation on consciousness and executive function has been well established. In high-altitude hypoxic environments, chronic inflammation and oxidative stress lead to reduced synaptic plasticity in the prefrontal cortex, resulting in attentional distraction and impaired working memory. Pro-inflammatory factors (such as IL-1β) inhibit the release of acetylcholine and norepinephrine, affecting the regulation of attention by the basal forebrain and brainstem.[39] Cytokines such as IL-6 and TNF-α cross the blood-brain barrier and modulate the hypothalamic-pituitary axis, thereby reducing non-rapid eye movement sleep (NREM) and contributing to sleep fragmentation, indirectly affecting attention and clarity of consciousness during wakefulness.[40] Inflammation has also been found to related with sleep. For example, in patients with chronic insomnia, elevated IL-6 levels are significantly associated with diminished deep sleep.[39]

Therefore, our study investigates the dynamic interaction between attention and sleep within high-altitude hypoxic stress, examining biological underpinnings and mental health implications for local residents. We propose that sleep impacts orienting attention, which in turn influences executive control via erythrocyte-induced inflammation. This biological mechanism is thought to also affect consciousness speed, modifying executive control's effects on sleep and mental well-being. Furthermore, studies show increased N1 and P3 amplitudes under hypoxia, affecting posterior orienting and executive control during attention tasks.[8] We aim to assess how plateau sleep affects these event-related potentials. We will also explore how sleep mediates the resource competition between orienting and executive functions in a low oxygen environment, as established by prior research.[41,42]

Materials and Methods
Participants
G-Power (Version 3.1) guided our sample size to detect an expected effect of d = 0.53, based on the impact of sleep deprivation on attention with a two-tailed *t*-test at α = 0.05 and β = 0.8, resulting in a target of 128 participants.[43] To account for potential data exclusions, we recruited 140 han Chinese juniors from Tibet University, originally from lowland areas (< 1500 m), without sleep or significant health issues. After excluding one individual for sleep medication use, six for low breaking continuous flash suppression (b-CFS) task accuracy, five for poor electroencephalography (EEG) data quality, and two with blood phobia, 126 participants (age: 22 ± 1.27 years; 70 females) remained in the study.

Experimental Procedures and Measurement

Experimental Procedures

Initially, participants underwent the Symptom Check-List-90 (SCL-90), Pittsburgh Sleep Quality Index (PSQI) assessments and b-CFS experiment in a dark, shielded space. This was followed by the Attention Network Test (ANT) experiment with concurrent EEG recording in a dim room. Physical examinations were conducted the subsequent day at Tibet General Hospital (Figure 1).

SCL-90

The SCL-90, developed by Derogatis et al, assessed participant health status through 90 items spanning ten factors including somatization, obsessive-compulsive symptoms, and others, which is free to use for non-commercial research and educational purposes.[44] Items are rated from 0 (never) to 4 (severe), with an overall General Symptom Index reflecting the average of all scores.

PSQI

The PSQI by Buysse et al was used to evaluate participants' perceived sleep quality through 19 self-rated items, which can be used freely for non-commercial research and educational purposes.[45] These are organized into seven components—each scored equally from 0 to 3—that aggregate into an overall score, encompassing aspects like sleep duration and disturbances. Higher PSQI scores indicate worse sleep quality.
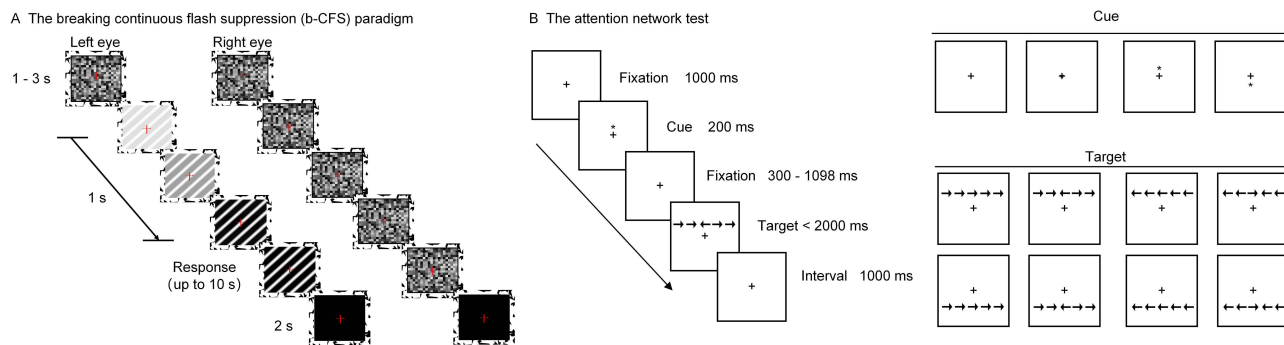
b-CFS

Stimuli were generated with Matlab R2013a (The MathWorks, Inc., Natick, USA), including a standard dynamic noise pattern and the test figure (grating with different tilt angles ranging from 70° to 110° at a step size of 0.5°) which were presented on a 19-inch Mitsubishi Diamond Pro monitor (1280 pixels 91024 pixels at 100 hz). The head of the participant was placed on a chinrest, and the distance from eyes to the monitor was 75 cm. The dynamic pattern was presented to the left and right sides at the beginning of the experiment using Psychtoolbox (http://psychtoolbox.org/) at full contrast for 1 s – 3 s. Then the dynamic pattern kept being projected to one eye at full contrast, at the same time, the test figure was projected to the other eye. The contrast of the test figure quickly raised from 0 to 100% in 1 s, then remained constant within 10 s until the participant made a judgment by pressing the left or right arrow key about the direction of the tilted gratings in test figure If no response was made in 10 s, the next trial would start after an interval of 2 s (Figure 2A).

ANT and EEG Recordings

The ANT involves phases with fixation, cues, and targets.[46] With three cue types—no cue, center cue (asterisk at fixation), and spatial cue (asterisk where target appears)—and two target configurations, the ANT assesses alerting,
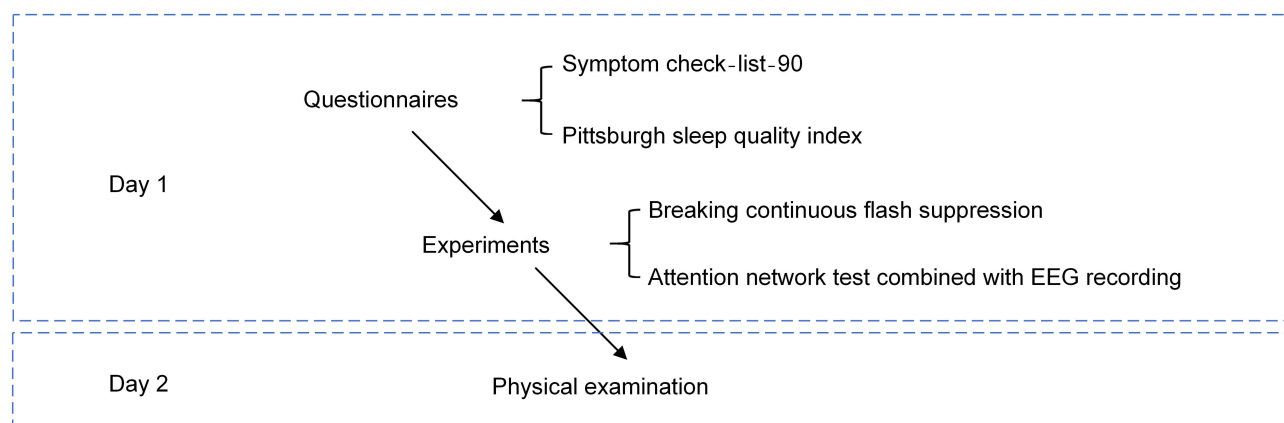
Figure 1 Graphical description of experimental procedures. Over two days, the experiment had subjects complete questionnaires and behavioral tests on day one, and undergo medical examinations on day two.

Figure 2 Graphical presentation of the experimental paradigm. (**A**) In the b-CFS paradigm, dynamic patterns at full contrast flash on either side for 1 – 3 seconds. Simultaneously, a test figure's contrast increases sharply from 0 to 100% in 1 second on the corresponding opposite side for the other eye, and stays consistent for up to 10 seconds until participants discern the tilt direction. (**B**). The ANT paradigm begins with a 1000 ms fixation cross, succeeded by a cue or fixation lasting 200 ms. Following a random interval of 300–1098 ms, a target appears; participants must indicate the central arrow's direction promptly and precisely within 1000 ms, leading into a subsequent 1000 ms pause before the next trial.

orienting, and executive control. Targets are rows of five arrows that can point congruently or incongruently. Each trial begins with a 1000 ms central fixation cross, followed by a 200 ms cue period and a random interval before the target presentation. Participants quickly judge the central arrow's direction. Post-response, a 1000 ms pause precedes the next trial.

Participants completed six sessions of 108 trials each during a 30-min test (Figure 2B), with cues and targets distributed randomly. A 64-channel ANT Neuro system recorded EEG at 500 hz. Vertical EOG was captured below the left eye, CPz served as the reference electrode, and FCz as ground. Electrode impedance was kept below 5 kΩ.

Physical Examination

On the second day, the participant underwent a standardized medical examination at the China People's Armed Police Force Tibet General Hospital. This included:

Liver function tests: ALT, TP, ALB, GLB, AG, TBIL, DBIL, UBIL.

Renal function tests: Urea, CREA, UA.

Complete blood count (CBC): WBC subtypes (NEUT, LYMPH, MONO, EO, BASO with absolute counts and percentages), RBC indices (HGB, HCT, MCV, MCH, MCHC, RDW), and platelet parameters (PLT, PCT, MPV, PDW, P-LCR).

Data Analyses

ANT Behavioral Analysis

For each participant and condition, we calculated accuracy and mean response times (RTs) for correct answers. We excluded trials with incorrect direction responses or extreme RTs beyond 3 standard deviations from the grand mean. The alerting score was derived by subtracting the central cue RT mean from the no-cue RT mean; a higher score indicates stronger alerting. The orienting score came from the spatial cue RT mean minus the central cue mean, with a higher score signifying enhanced orienting. The executive control score was obtained by subtracting congruent condition RTs from incongruent ones; smaller values denote superior executive control.

b-CFS Behavior Analysis

The reaction time of consciousness-breaking was calculated as the interval between two time points. The first time point is when the contrast of the test image overcame the suppression noise (the dynamic pattern). The second time point is when the participant responded. The accuracy is the percentage of trials in which the participant responded correctly out of all trials. Participants with accuracy below 80% were removed from following analysis.

Latent Class Analysis (LCA) and Regression Mixture Model (RMM)

Using MPLUS (Version 7.3), LCA was conducted to uncover hidden patterns in objective sleep conditions. Excluding the use of sleep medication, we assessed the six PSQI components. In order to correctly evaluate the model fitness based on the index of adjusted Bayesian Information Criterion (aBIC), each group should contain at least 50 samples.[47] Therefore, we established models containing one or two latent classes and tested them. The model's fitness was determined by evaluating the Bayesian Information Criterion (BIC), entropy, and the adjusted likelihood ratio test to select the most suitable interpretation.[48,49]

Following this, RMMs examined predictors and outcomes associated with latent sleep conditions. Health statuses and attention networks' influence on latent sleep conditions were probed using a three-step distal regression in MPLUS (Version 7.3).[50] Additionally, the effects of latent sleep conditions on health status and attention networks were analyzed through the adjusted BCH method.[50] Odds ratio (OR) is used to measure the association that quantifies how the presence of a particular predictor affects the likelihood of belonging to one latent class versus another. If OR > 1, that means the variable renders participants more likely to be included in the target group compared to the reference group.

Multilevel Mediation Analysis

To investigate the attention-sleep relationship, we employed MPLUS software (Version 7.3) to construct a multilevel mediation model integrating latent and observed variables.[51] Model acceptability was judged based on fit indices: $\chi^2/df <$ 3.0, Root Mean Square Error of Approximation (RMESA) < 0.08, Comparative Fit Index (CFI) and Tucker–Lewis Index (TLI) > 0.9, and Standardized Root Mean Square Residual (SRMR) < 0.08. Ensuring validity, bootstrap analysis utilized 1000 samples. Indirect effects were considered significant if their 95% percentile or bias-corrected bootstrapped Confidence Intervals (CIs) did not include zero.

EEG Preprocessing

Data preprocessing utilized Matlab R2013a and the eeglab2019_0 toolbox.[52] The EEG signals underwent a bandpass filter from 0.1 to 40 hz, followed by artifact rejection in each epoch for non-physiological spikes. Independent Component Analysis (ICA), enhanced with the ICLabel extension and manual curation, was applied to exclude eyeblink, movement, and cardiac artifacts. This was succeeded by re-referencing to the average of all scalp channels and selecting specific epochs for analysis. Epochs locked to cue onset were assessed within a time frame of −500 ms pre-stimulus to 1000 ms post-stimulus, referencing −200 ms to 0 ms as the baseline, with identical parameters applied to target onset locked epochs. Epochs with signal amplitudes beyond ±100 μV were discarded.

Time-Domain Analysis

Studies indicate that the P1, N1, P2, and N2 ERP components are responsive to the spatial locations of visual stimuli, with N2 and P3 serving as indicators of cognitive control during conflict resolution tasks.[53–56] Fan et al cue-locked measures for alerting/orienting networks, while executive network measures were target/response-locked.[57]

In our study, P1, N1, P2, and N2 amplitudes representing alerting and orienting activity were derived from average single-trial amplitudes at O1, Oz, O2, P3, Pz, and P4 electrodes. Time windows for these components were set to 80 – 150 ms for P1, 150 – 200 ms for N1, 200 – 250 ms for P2, and 250 – 300 ms for N2, post-cue onset. The P3 amplitude was measured in relation to target onset within 350 – 700 ms at CFz, Cz, and Pz electrodes. These ERP components were calculated as described below:

Alerting = component center cue – component no cue;
Orienting = component spatial cue – component center cue;
Executive control= component incongruent target – component congruent target;

Source Analysis

To trace the origin of Event-Related Potentials (ERPs), we used standardized low-resolution brain electromagnetic tomography (sLORETA).[58] Initial electrode positions for 61 channels were mapped from record arrays, leading to a transformation matrix tailored for ERP conversion to sLORETA inputs.[59] We conducted paired *t*-tests to discover the neural sources of variance in orienting P1 between two sleep groups within 140 – 150 ms following cue onset. P-values

A

B
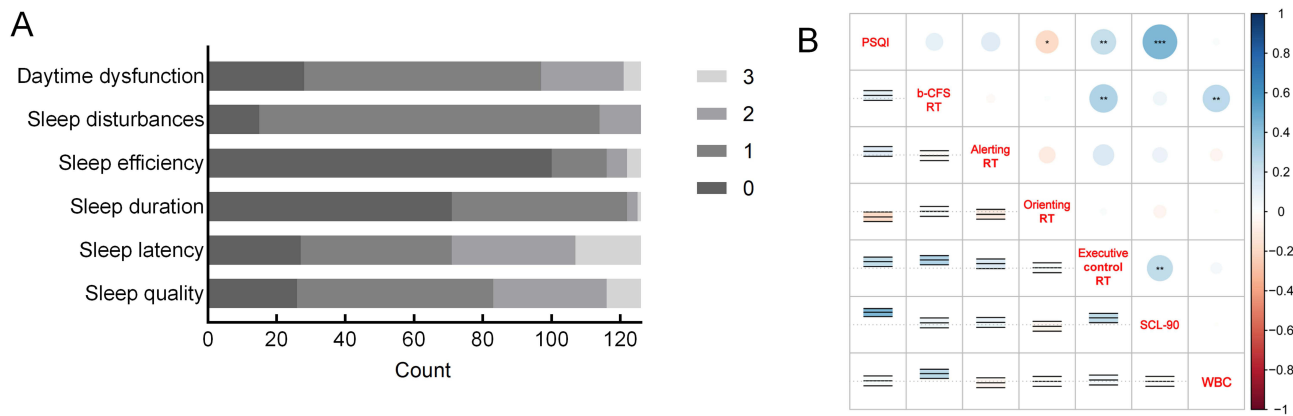
Figure 3 Descriptive statistics of sleep and attentional EEG. (**A**) PSQI component scores are represented, where higher values indicate poorer sleep quality. (**B**) The matrix displays correlations between variables related to sleep, attention, b-CFS, health status, and physiological functions. Pearson's correlation coefficients are shown in the upper triangle, with circle size denoting the strength of each correlation. The lower triangle presents the confidence intervals for these coefficients. The upper and lower black line represent the upper and lower boundary of the confidence interval. The grey dotted line in the middle depicts neutrality with blue color inside indicating positive correlations and red color inside signifying negative ones. Levels of significance are noted by asterisks: *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

underwent correction via Statistical non-Parametric Mapping (SnPM) to ensure robust analysis, with 5000 randomizations.

Statistical Analyses

Pearson correlation coefficient was used to calculate the correlation using the Statistical Package for the Social Sciences (SPSS, Version 21.0; SPSS Inc., Chicago, IL).[60] G*Power (Version 3.1) was used to analyze the calculation power of independent *t*-test.

Results
Descriptive Statistics and Correlational Analyses

Figure 3A summarizes the PSQI component scores, indicating sleep condition quality with higher scores denoting poorer status. The total PSQI score averaged 5.40 (SD = 2.83). Physiological function, behavioral performance, and health status means are detailed in Table 1. Pearson's correlation analysis uncovered interconnections among sleep quality, attention network efficiency, b-CFS RTs, health status, and physiological metrics (Figure 3B). Notably, a significant negative

Table 1 Descriptive Statistics of Physiological Functions, Behavioral Performance and Health Status

	Mean	SD		Mean	SD
Physiological functions			*Health status*		
RBC (10^{12}/L)	5.30	0.51	Somatization	16.47	3.61
HGB (g/L)	163.31	19.94	Obsessive-compulsive	19.21	5.08
HCT (%)	46.63	4.80	Interpersonal sensitivity	15.10	4.83
WBC (10^9/L)	7.38	7.57	Depression	20.77	6.22
NEUT# (10^9/L)	3.35	1.32	Anxiety	15.02	4.32
LYMPH# (10^9/L)	2.50	0.60	Hostility	8.85	2.71
Behavior performance			Phobic Anxiety	9.43	2.81
b-CFS RT (s)	1.50	0.46	Paranoid Ideation	9.07	2.66
Alerting RT (ms)	8.68	11.48	Psychoticism	15.98	4.33
Orienting RT (ms)	58.66	19.03	Others	11.15	3.14
Executive control RT (ms)	89.18	30.44	SCL-90	141.06	32.95

Note: The italicized words represent the category that the following indices belong to.
Abbreviations: SD, standard deviation; RBC, red blood cell count; HGB, hemoglobin; HCT, hematocrit; WBC, white blood cell count; NEUT#, neutrophil count; LYMPH#, lymphocyte count; RT, reaction time.

correlation existed between PSQI scores and orienting RTs, while a positive one was observed between PSQI scores and executive control RTs. Both PSQI and executive control RTs were positively associated with SCL-90 overall scores, additionally, b-CFS RTs were positively related to both executive control RTs and WBC counts.

Two Different Patterns of Sleep From LCA

LCA was used to discern sleep patterns among participants, with model fit indices presented in Table 2. Two latent classes yielded lower Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and sample-size adjusted BIC (aBIC). Crucially, both Lo-Mendell-Rubin (LMR) and Bootstrapped Likelihood Ratio Test (BLRT) statistics were significant for the two-class solution, with an entropy value of 0.831 indicating reliable classification. Balancing simplicity with precision, we ultimately adopted the two-class model to characterize sleep conditions.

Interaction of Health Status and Attention With Sleep Patterns

RMM was employed to discern how the latent sleep profiles related to other variables. According to predictive outcomes in Table 3, all subscales and the total SCL-90 score were significant predictors of sleep condition classification, signifying a link between health status and group belonging. Attention network analyses showed that it was orienting and executive control, not alerting, that influenced sleep patterns. Evaluating the multinomial logistic regression odds ratios (OR), we

Table 2 Model Fitness of LCA

Number of Latent Classes (N=126)	k	AIC	BIC	aBIC	LMR(p)	BLRT(p)	Entropy	Class Proportions
1	17	1513	1561	1507	–	–	–	1.00
2	35	1440	1539	1429	0.0001	0.0000	0.831	0.52/0.48

Abbreviations: AIC, Akaike information criterion; BIC, Bayesian information criterion; aBIC, adjusted Bayesian information criterion; BLRT, bootstrapped LRT; LMR, Lo-Mendell-Rubin LRT; LRT, likelihood ratio test.

Table 3 Predicting Sleep Condition From Health Status and Attention Networks

Predictive Variables	Poor and Inefficient Sleep			Good and Efficient Sleep		
	Coefficient	S.E.	OR	Coefficient	S.E.	OR
Health status						
Somatization	0.208**	0.071	1.231	−0.208**	0.071	0.812
Obsessive-Compulsive	0.182***	0.051	1.200	−0.182***	0.051	0.833
Interpersonal Sensitivity	0.172***	0.050	1.188	−0.172***	0.050	0.842
Depression	0.159***	0.049	1.172	−0.159***	0.049	0.853
Anxiety	0.243***	0.057	1.275	−0.243***	0.057	0.784
Hostility	0.299**	0.102	1.349	−0.299**	0.102	0.741
Phobic Anxiety	0.310**	0.113	1.364	−0.310**	0.113	0.733
Paranoid Ideation	0.357**	0.122	1.429	−0.357**	0.122	0.700
Psychoticism	0.279***	0.065	1.322	−0.279***	0.065	0.756
Others	0.606***	0.156	1.833	−0.606***	0.156	0.546
SCL-90	0.037***	0.008	1.038	−0.037***	0.008	0.963
ANT reaction time						
Alerting	−0.013	0.017	0.987	0.013	0.017	1.013
Orienting	−0.025*	0.012	0.975	0.025*	0.012	1.025
Executive control	0.014*	0.007	1.014	−0.014*	0.007	0.986

Note: Poor and inefficient sleep is the reference category. Coefficient, multinomial logistic regression coefficient; S.E., standard error of the coefficient; OR, odds ratio. *p < 0.05, **p < 0.01, ***p < 0.001. The italicized words represent the category that the following indices belong to.

Table 4 Evaluating the Effects of Latent Sleep Condition on Health Status and Attention Networks

Outcome Variables	Poor And Inefficient Sleep		Good and Efficient Sleep		Overall χ^2
	Mean	S.E.	Mean	S.E.	
Health status					
Somatization	17.482	0.479	15.159	0.426	11.631***
Obsessive-Compulsive	20.895	0.674	17.027	0.570	16.954***
Interpersonal Sensitivity	16.586	0.669	13.189	0.510	14.286***
Depression	22.767	0.868	18.192	0.632	15.836***
Anxiety	16.557	0.624	13.045	0.369	20.201***
Hostility	9.627	0.379	7.845	0.284	12.392***
Phobic Anxiety	10.203	0.400	8.429	0.283	11.391***
Paranoid Ideation	9.886	0.363	8.020	0.292	14.125***
Psychoticism	17.652	0.608	13.832	0.388	24.241***
Others	12.600	0.377	9.280	0.357	36.558***
SCL-90	154.254	4.489	124.018	3.148	26.493***
ANT reaction time					
Alerting	7.883	1.641	9.716	1.315	0.667
Orienting	54.923	2.321	63.484	2.668	5.304*
Executive control	94.457	4.048	82.372	3.848	4.170*

Note: S.E., standard error of the coefficient; *$p < 0.05$, ***$p < 0.001$. The italicized words represent the category that the following indices belong to.

inferred that participants with lower SCL-90 scores (OR = 0.963), shorter executive control RTs (OR = 0.986), and longer orienting RTs (OR = 1.025) were likelier to fall into the high-efficiency sleep category.

Outcome analysis, detailed in Table 4, found significant health status differences between the sleep groups. The high-efficiency sleep group showed substantially lower SCL_90 scores (χ^2 (1) = 26.493, $p < 0.001$), indicating better overall health. Notably within attention networks, the orienting RT was longer (χ^2 (1) = 5.304, $p = 0.021$) and the executive control RT was shorter (χ^2 (1) = 4.170, $p = 0.041$) for those with high-efficiency sleep, implying such sleep may enhance orienting and executive control abilities without affecting alerting. These findings point to a potential bidirectional interplay between sleep and attention networks, along with health status.

Figure 4 illustrates that the first class had higher scores in sleep quality, latency, and efficiency compared to the second class, indicating better perceived sleep quality and quicker sleep onset in the latter. Lower incidences of sleep disturbances and daytime dysfunction suggest fewer sleeping issues and enhanced daytime alertness in the second
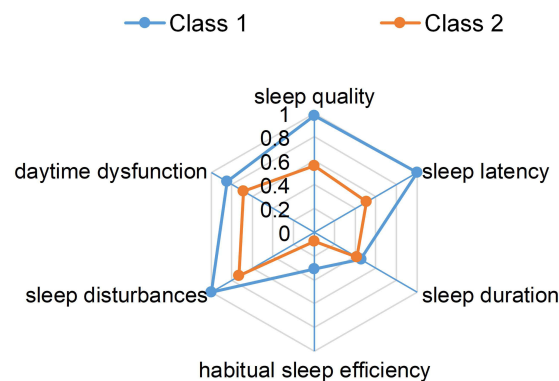
Figure 4 Profile of sleep condition. Probability of sleep quality, latency, duration, efficiency, and daytime dysfunction of two sleep groups.

class. Thus, the classes were designated as "low-efficiency" and "high-efficiency" sleep groups, comprising 52% and 48% of participants, respectively.

## The Mechanism Underlying the Effects of Sleep on Attention

Considering the association between sleep profiles and RTs of orienting and executive control, alongside correlations found between PSQI scores and these RTs, we aimed to further investigate the impact of sleep on orienting and executive function, including potential biological influences. Structural equation modeling demonstrated that erythrocyte-induced changes in WBC count could adversely affect sleep quality, subsequently impacting executive control RT (indirect effect = 0.007, bias-corrected bootstrapped 95% CI = [0.000, 0.024]). Additionally, the effect of sleep quality on executive control RT was partially mediated by the amplitudes of P1 and N1 components associated with orienting (indirect effect = 0.001, bias-corrected bootstrapped 95% CI = [0.000, 0.003]). These pathways are represented in Figure 5. The linear relationship of the model was verified by the scatterplot inspection with locally estimated scatterplot smoothing (LOESS) smoothing and quadratic term test (Supplementary Materials, Supplementary Figure 1 and Table 1). The model's fit indices were satisfactory (χ^2 = 9.155, df =10, CFI = 1.000, TLI = 1.004, RMSEA = 0.000, SRMR = 0.018), supporting the hypothesis that erythrocyte-induced WBC alterations mediate the effects of sleep on attentional networks.

Orienting P1 Differs Significantly in Two Sleep Groups and This Difference Lies Mainly in the Insula

An independent t-test showed a significant difference in the amplitude of the orienting P1 component, which was notably higher in the high-efficiency sleep group (Mean = 0.36, S.E. = 0.61) compared to the low-efficiency group (Mean = 0.16, S.E. = 0.43). Statistical analysis yielded a value of $t_{(105.885)}$ = −2.114 with p = 0.037 (Bonferroni corrected p = 0.111) and an effect size measured by Cohen's d at 0.38, reflecting a moderate difference (Figure 6A). G*Power revealed the calculation power is 0.39. Source localization analysis revealed that, within the time window from 140 ms to 150 ms, the insula (specifically in the Brodmann area 13 with MNI coordinates x = −40, y = 15, z = 10) exhibited the greatest discrepancy between the two sleep groups, reaching a peak of t = 6.43, indicating a highly significant contrast (p < 0.001) as illustrated in Figure 6B.

## The Mechanism Determining the Influences of Attention on Sleep

Multilevel mediation models were constructed to explore how orienting and executive control may influence sleep, with sleep classification being predicted by the RT of these attention networks. Further, since the PSQI scale correlation with RTs suggests a deeper relationship, these models also considered biological factors.
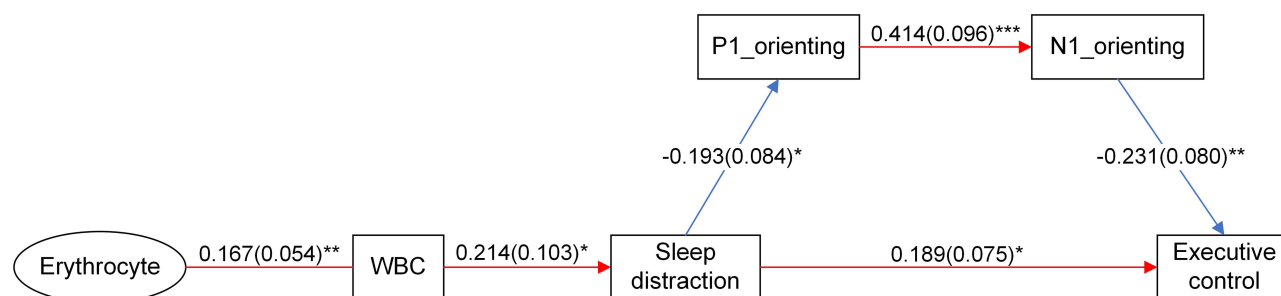
Figure 5 The pathway by which sleep affects attention. The multi-level mediation analysis is depicted through path diagrams, illustrating the relationships between the latent variable erythrocyte (composed of RBC count, hemoglobin or HGB, and hematocrit or HCT levels), WBC count, sleep distractions, P1_orienting amplitude, N1_orienting amplitude, and executive control RT. Path coefficients are provided alongside their standard errors. In the diagram, a red line corresponds to positive regression weights, indicating that an increase in the predictor variable correlates with an increase in the outcome variable. Conversely, a blue line indicates negative regression, where higher values of the predictor correspond to lower values of the outcome variable. Significance levels are marked by asterisks next to the path coefficients: a single asterisk denotes p < 0.05, two asterisks signify p < 0.01, and three asterisks indicate p < 0.001, reflecting increasing levels of statistical significance.

A

B
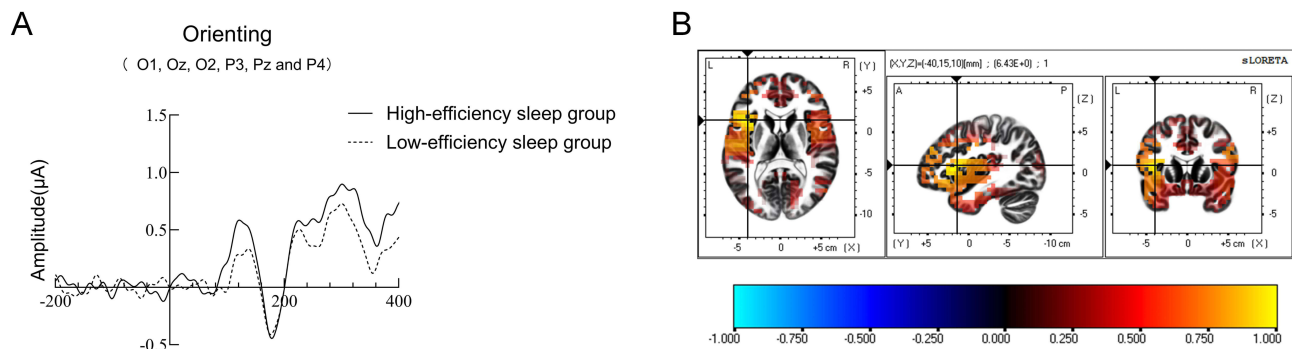
Figure 6 Source of orienting P1 differences in two sleep groups. (**A**) A comparison of the mean power at electrodes O1, Oz, O2, P3, Pz, and P4 during the orienting condition shows the high-efficiency sleep group (represented by a solid line) exhibits greater activity than the low-efficiency sleep group (indicated by a dotted line). (**B**) The sLORETA image depicts the neural localization of differences in orienting P1 component responses between the two sleep groups, within 140 ms to 150 ms following cue onset. Areas where the high-efficiency sleep group shows greater activation than the low-efficiency group are highlighted in yellow, while regions with lower activity in the high-efficiency group are shown in blue.
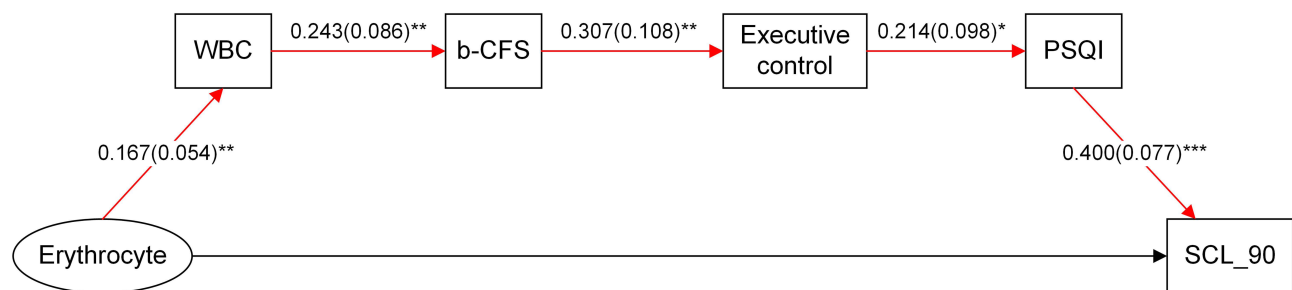

Figure 7 The pathways through which attention impacts sleep. The depicted path elucidates how the erythrocyte index influences mental health status through a chain of mediating factors: white blood cell (WBC) count, consciousness-breaking reaction time (b-CFS RT), executive control reaction time (RT), and the Pittsburgh Sleep Quality Index (PSQI). The path coefficients are displayed alongside corresponding standard errors in parentheses. In this visual model, red lines signify pathways with positive regression weights, indicating that an increase in the predictor variable is associated with an uptick in the outcome variable. Conversely, black lines denote pathways where the regression is not statistically significant. Significance levels for each path coefficient are coded by asterisks, with *p < 0.05, **p < 0.01, ***p < 0.001 indicating increasing degrees of statistical confidence.

Figure 7 displays that erythrocyte levels directly affect WBC count, which then mediates the impact of executive control RT on PSQI score. This chain of effects extends to the Symptom Checklist-90 (SCL-90) score, reflecting mental health status (indirect effect = 0.001, bias-corrected bootstrapped 95% CI = [0.000, 0.004]). No significant path was found from orienting to executive control. Scatterplot inspection with LOESS smoothing and quadratic term test validated the linear relationship of the model (Supplementary Figure 2 and Table 2). Figuratively depicted path coefficients in Figure 7 suggest solid model fit (χ^2 = 9.131, df = 10, CFI = 1.000, TLI = 1.004, RMSEA = 0.000, SRMR = 0.018).

Collectively, the findings imply executive control is a key intermediary between sleep and mental health, influenced biologically by erythrocyte-mediated WBC changes and functionally related to the speed of conscious breaking.

The Competition Between Alerting and Executive Control Exists in the Good and Efficient Sleep Group

Previous studies have suggested that heightened alerting can detrimentally affect executive control performance. In contrast, our research found a positive correlation between alerting and executive control within the high-efficiency sleep group (r = 0.273, p < 0.05, as shown in Figure 8). This association was not observed in the low-efficiency sleep group, where the relationship did not reach statistical significance (r = 0.126, p > 0.05).
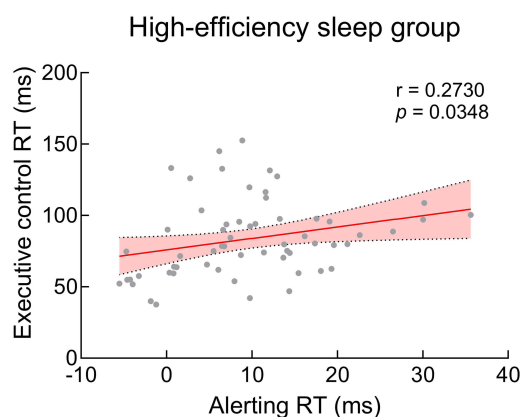
Figure 8 The correlation between the reaction time (RT) of alerting and executive control. Alerting RT exhibits a positive correlation with executive control RT. The regression analysis is visually represented by a red line, with the 95% confidence interval shaded in pink.

Discussion

The interplay between sleep and attention—both states marked by information suppression[1] — was examined using structural equation modeling in a population enduring chronic hypoxic stress. While the impact of sleep on attention is established, this study probes the reverse: how attention may influence sleep.[17] Our results revealed that executive control is not merely reactive to sleep but interacts with it via erythrocyte-influenced immune pathways. In essence, inflammation driven by RBC characteristics directly affected orienting responses and executive functioning, requiring an interruption of consciousness to further modulate how executive control influences sleep patterns. Additionally, the role of executive control in sleep linked to mental health outcomes, where individuals with efficient sleep demonstrated larger orienting P1 amplitudes alongside a dynamic tension between alerting and executive control processes. This research provides a pioneering neurobiological exploration into how attention networks may govern sleep within a hypoxic context. In examining a hypoxic environment, our study identified two distinct sleep patterns—high-efficiency and low-efficiency sleep. Individuals with high-efficiency sleep experienced faster sleep onset, superior perceived sleep quality, fewer sleep disturbances, and improved daytime functioning.[24] Crucially, we found that these sleep types influenced orienting and executive control in a bidirectional manner.

Our findings suggest that the relationship between sleep and executive control functions biologically hinges on inflammation induced by erythrocyte changes, consistent with literature noting increased erythrocyte production and corresponding inflammatory markers under stress.[23,61] In our research, erythrocyte is composed of RBC count, HGB, and HCT levels. HGB has already been discovered to promote immune response by activates toll-like receptor 4.[37] However, we did not measure toll-like receptor 4 but discovered a positive regulation effect of erythrocyte on WBCs. This may be explained by that HGB alleviates tissue hypoxia by forming hemoglobin bodies (Hedy) to store oxygen, thereby indirectly suppressing the excessive release of inflammatory factors and potentially regulating the activity of WBCs.[62] This finding not only reinforces our prior findings that the capacity of oxygen transport is a fundamental physiological mechanism influencing human attention performance at high altitudes by modulating inflammatory processes and heart rate variability, but it also broadens our understanding by identifying erythrocyte-induced inflammatory processes, especially HGB-induced WBCs, as the key mechanism driving the reciprocal relationship between sleep and attention.[32] But it could also be because that red blood cells help regulate sleep quality by clearing inflammatory mediators (such as CpG DNA) and releasing anti-inflammatory molecules (such as adenosine). On the other hand, lack of sleep enhances red blood cell-mediated inflammation through PGD2 signaling, forming a positive feedback loop.[63,64]

These erythrocyte-mediated effects implicate an interplay where inflammation may disrupt both consciousness and sleep quality. Although we could not confirm whether it was also modulated by IL-6 and TNF-α,[40] but this gives directions to future research and supports the embodied cognition framework where the body's biological state influences cognitive functions.[65] In terms of attentional processing in visual tasks, our results resonate with previous findings where P1 is linked to spatial awareness and N1 to the discrimination process,[53,55] suggesting sleep disturbance diminishes

sensitivity to cue locations and hampers conflict resolution, whereas executive control directly impacts sleep quality—a relationship hinting at a hierarchical effect of sleep on attentional networks.

Moreover, we posit that one's awareness of physiological shifts could modulate how executive control regulates sleep, ultimately affecting mental health.[66] Thus, the intricate dance between sleep, attention, and biological mechanisms presents a compelling narrative for future explorations into this interconnected domain.

Individuals experiencing high-efficiency sleep showed not only quicker orienting responses but also larger P1 amplitudes (not significant but with low calculation power) in response to the spatial cues than those with low-efficiency sleep, an effect primarily attributed to the insula's activity. The insula is integral to sensorimotor processing and forms part of the "salience network", particularly where the dorsal anterior section integrates external sensory data with internal bodily states, modulating brain networks like the default mode network through dynamic switching.[67] Therefore, the insula in individuals with high-efficiency sleep may be more adept at assimilating these diverse inputs, which could account for their improved orienting performance.

Moreover, we found that in the high-efficiency sleep group, there exists a competitive dynamic between alerting and executive control functions. Past studies indicated that increased alerting might adversely impact executive control as it potentially heightens awareness towards both targets and distractors, obstructing conflict resolution, a notion corroborated by research in high-altitude settings.[8,41,42] Hence, in hypoxic environments typical of high altitudes, effective sleep management can possibly preserve this competitive balance between alerting and executive control.

This article's pivotal insight lies in demystifying the interplay between sleep and executive control from a biological vantage point while considering the implications on mental health. Maintaining a balanced physiological response in hypoxic conditions is crucial, promoting better sleep, orienting abilities, executive functioning, and well-being. More profoundly, the studied interrelation of sleep and executive control suggests that they mirror the yin and yang concepts from Chinese philosophy—two distinct yet interconnected forms of cognitive suppression.[1] Optimal sleep can enhance orienting and help maintain a necessary balance between alerting and executive control, enabling the efficient distribution of attentional resources for superior cognitive performance.

This work also sheds lights on clinical interventions from the following 4 aspects:

1. Intervention Targets for Brain Function Protection: This study highlights the mediating role of P1 and N1 amplitudes, suggesting that they could be potential targets for neuromodulation techniques like transcranial electrical stimulation (tES). In high-altitude environments, interventions focusing on these neuroelectrophysiological markers may help improve sleep and cognitive function.
2. Early Warning for Mental Health Risks: Sleep disturbances and cognitive decline are common in high-altitude regions. Monitoring sleep parameters along with indicators of directed attention (such as P1 amplitude) could serve as an early warning system, allowing timely interventions to reduce mental health risks.
3. Training Strategies for Environmental Adaptation: Since executive control can regulate sleep through feedback mechanisms, cognitive training programs could be designed to strengthen executive control abilities in high-altitude populations. This may improve sleep quality and promote better adaptation.
4. Integration of Multimodal Intervention Strategies: A comprehensive approach combining sleep hygiene education, neuromodulation, and anti-inflammatory therapies should be developed to protect brain function in high-altitude environments. This integrated strategy targets multiple pathways to achieve optimal outcomes.

For forthcoming studies, there are several considerations to enhance the understanding of sleep and attention relationships:

1. Baseline Measurement: In order to validate the adaptation effect, it's better to measure the sleep, function of attention network, liver function, kidney function, blood routine and mental health before they immigrate to high-altitude regions.
2. Incorporation of Objective Measures: It is essential to use objective measurement tools like polysomnography or actigraphy to capture detailed SWS (slow-wave sleep) characteristics and obtain a more comprehensive assessment

of sleep architecture.[68] In this way, we can compare the slow-wave oscillation during sleep with that during orienting and executive control attention to figure out the underlying interacting neural mechanism.

3. Comparison with Control Group: Recruiting a control group from non-hypoxic regions would provide comparative data, facilitating a deeper investigation into how hypoxia may specifically alter the interplay between sleep and attention functions, however, we need to control potential confounding factors, for example, the laboratory environment, the device, the diet of participants (which may influence physiological condition). Besides, we can also recruit participants of medium- and high- altitudes (e.g., 2900 m, 3700 m, 4200 m) to make comparison.

4. Recruitment Groups Other than College Students: To improve the generalizability of our research, we need to recruit participants with more diverse background, for example, people who are over 30 and have a job.

5. Refined Experimental Paradigms for Orienting: Modifying experimental paradigms to include lateralized spatial cues—distributed or pointing left or right—can offer a more nuanced analysis of alpha oscillations associated with attentional orienting processes.[69]

6. Including fatigue as an influencing factor for the attention networks performance: Although there is a self-paced rest after each block and this method can capture the fluctuation of attention close to real-life condition, it is still worthwhile to analyze the effect of fatigue on attention networks performance, especially in hypoxic high-altitude areas where fatigue induced by the hypoxia is unable to neglect and might interact with the fatigue of doing cognitive tasks.[70]

7. Measuring of pro-inflammatory cytokines: Considering cytokines such as IL-6 and TNF-α might influence sleep and attention,[40] it deserves to explore whether they also contribute to the underlying biological mechanism.

Future research addressing these points can broaden the scope of current findings and contribute to a more robust understanding of the physiological and cognitive implications of sleep quality and its interaction with attention networks.

Conclusion

Our investigation revealed that sustained hypoxic conditions induce changes in RBC characteristics, which in turn initiate an immune response that regulates the interplay between sleep quality and executive control functions. The impact of sleep on executive abilities is mediated by variations in orienting amplitudes, whereas the influence of executive control on sleep quality is reflected in the individual's mental health. Individuals with high sleep efficiency demonstrated enhanced abilities in both orienting and executive tasks, indicative of a more strategic distribution of attentional capacities. Ultimately, this study sheds light on the complex dynamics between sleep and attentional networks under chronic hypoxia and the neurobiological underpinnings of these associations.

Data Sharing Statement

The data used to support the findings of this study are available from the corresponding author upon request. The data can only be for research use. If the associated research is to be published, the statement "The data and code were acquired from the Plateau Brain Science Research Center, Tibet University/South China Normal University, Lhasa 850012, China" is required in the paper.

Ethics Approval and Informed Consent

Written informed consent was provided by participants before they took part in the experiments. The study was approved by the local Ethics Committee of Tibet University and followed the Declaration of Helsinki.

Author Contributions

Conceptualization: De-Long Zhang. Data curation: Hai-Lin Ma, Xiao-Juan Xue, Ze-Feng Li, Rui Su, Jin-Guo Zhu, Hao Li, Ming Liu. Formal analysis: Chun-Yan Shi, Xiao-Yan Huang, Nian-Nian Wang, De-Long Zhang. Funding acquisition: De-Long Zhang, Hai-Lin Ma. Investigation: Chun-Yan Shi. Methodology: Chun-Yan Shi, De-Long Zhang. Software: Chun-Yan Shi. Supervision: De-Long Zhang. Validation: Xiao-Juan Xue, Ze-Feng Li. Visualization: De-Long Zhang. Writing–original draft: Chun-Yan Shi. Writing–review&editing: De-Long Zhang, Xiao-Juan Xue, Ze-Feng Li. All

authors have drafted or written, or substantially revised or critically reviewed the article; agreed on the journal to which the article will be submitted; reviewed and agreed on all versions of the article before submission, during revision, the final version accepted for publication, and any significant changes introduced at the proofing stage; agreed to take responsibility and be accountable for the contents of the article. Acknowledgments We would thank all the participants for their involvements in this work.

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Disclosure

The authors report no conflicts of interest in this work.

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