Overactive Performance Monitoring Resulting from Chronic Exposure to High Altitude

Hailin Ma; Yan Wang; Jianhui Wu; Hailan Liu; Ping Luo; Buxin Han

INTRODUCTION: The neural mechanisms underlying the influence of chronic exposure to high altitude on performance monitoring are not clear. We investigated performance monitoring in the context of chronic exposure to high altitude.

METHODS: A go/no-go task was used to obtain event-related potentials (ERP). The error-related negativity (ERN), correct-related negativity (CRN), and error positivity (Pe) components were measured in high-altitude and low-altitude groups. The high-altitude group had lived at high altitude for 3 yr, but were born and raised at low altitude, whereas the low-altitude group had lived at low altitude only.

RESULTS: The ERN amplitudes were larger in the high-altitude group compared with the low-altitude group (-14.00 ± 8.34 μV vs. -7.82 ± 8.42 μV, respectively). Moreover, the CRN amplitudes were larger in the high-altitude group (3.51 ± 4.50 μV vs. 8.65 ± 3.23 μV, respectively). Group differences were not significant for the Pe component.

DISCUSSION: These results suggest that chronic exposure to high altitude can cause overactive performance monitoring in the high-altitude group, but the later stage of error monitoring was not influenced.

KEYWORDS: high altitude, go/no-go, error-related negativity, correct-related negativity, error positivity.

Ma H, Wang Y, Wu J, Liu H, Luo P, Han B. *Overactive performance monitoring resulting from chronic exposure to high altitude.* Aerosp Med Hum Perform. 2015; 86(10):860–864.

The largest and most important impact of living at high altitude is hypoxia, which is caused by a reduction of oxygen in the air and which affects cognition.[24] It has been well-documented that the hypobaric-hypoxic environment at high altitude affects the cognition of both permanent residents at high altitude and sojourners.[16,27] However, insufficient attention has been paid to people who were born and raised at low altitude, but have subsequently lived at high altitude for a long period of time; this group of subjects is considered to be more representative of the influence of high altitude.[25]

Chronic exposure to high altitude leads to deficits in cognition, such as in attention, memory, and executive functioning.[24] Neuropsychological data from world-class alpinists, who have chronic exposure to high altitude, show cognitive decline revealed by deficits in executive function.[20] Evidence from functional magnetic resonance imaging studies has shown that chronic high altitude exposure results in structural modifications of the prefrontal and cingulate cortices.[28] A positron emission tomography study has also found high altitude exposure to decrease regional cerebral glucose metabolism in the frontal cortex.[10]

Performance monitoring reflects one important aspect of core executive functioning that may underlie the regulation of emotions and behavior, consisting of the ability to evaluate performance and behaviors, and to signal for appropriate adjustments.[4,21] Evidence from neuroimaging studies demonstrates that the medial frontal cortex and the dorsal anterior cingulate cortex (ACC) are associated with performance monitoring.[17]

The event-related potentials (ERP) technique is effective for studying cognitive processes within a time resolution in the range of milliseconds. Three specific components are relevant in the context of response monitoring, namely error-related negativity (ERN), correct-related negativity (CRN), and error positivity (Pe).[3,26] The ERN component, which is believed to reflect activation in the ACC, is typically seen from 0 to 50 ms

From the Key Laboratory of Mental Health, Institute of Psychology, Chinese Academy of Sciences, Beijing, China.

This manuscript was received for review in January 2015. It was accepted for publication in June 2015.

Address correspondence to: Yan Wang or Buxin Han, 16 Lincui Road, Chaoyang District, Beijing 100101, China; wangyan@psych.ac.cn or hanbx@psych.ac.cn.

DOI: 10.3357/AMHP.4261.2015

following an incorrect behavioral response, with maximum amplitudes over the midline frontocentral scalp region.[6] The amplitude of ERN increases with the probability of error correction and with the degree of confidence that an error has occurred, reflecting a process of error monitoring and self-regulation.[18]

The CRN component during performance monitoring is a negative deflection following a correct behavioral response (between 0 and 150 ms after the response). The CRN amplitude peaks at frontal and central electrode sites, and is not as consistently observed as the ERN. The CRN might be due to stimulus-related artifacts or due to partial error processing on correct trials when stimulus ambiguity is high.[15] The CRN might also reflect the response evaluation process leading to error detection itself.[23] Alternatively, previous study has suggested that the CRN relates to alterations in the performance monitoring system.[2]

The third component during performance monitoring is a positive deflection following an incorrect behavioral response, termed the error-related positivity (Pe). The Pe potential is believed to be related to ACC activity.[14] Pe may reflect a later aspect of error processing reflecting conscious error recognition, or the emotional assessment of errors and their subjective motivational significance.[1]

Therefore, the high temporal resolution of ERPs can be used to identify distinct components of the cognitive processes that underlie performance monitoring. To our knowledge, however, there is no ERP study that evaluates performance monitoring following long-term exposure to high altitude.

The goal of the present study was to use ERP to address performance monitoring in the context of chronic exposure to high altitude using a go/no-go paradigm. As previous research has demonstrated that the performance monitoring neural networks are compromised by high altitude, and the prefrontal cortex and ACC structures are modified by high altitude,[28] we predicted that the effects of chronic exposure to high altitude would be found in ERP results. The amplitudes of ERN, CRN, and Pe components, whose sources are the prefrontal cortex and ACC areas, would be modified for the high-altitude group as compared with the low-altitude group.

METHODS

Subjects

There were 40 healthy college students, ages between 20 and 24 yr old, who took part in the experiment. All subjects signed an informed consent form before the experiment. The experiment was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Committee of the Institute of Psychology, Chinese Academy of Sciences. All of the subjects were right-handed by self-report, and had normal or corrected-to-normal vision. All were from the Han ethnic group and were born and raised near sea level in the first 18 yr of their lives. The results from six subjects were not included in the analysis because of too few false alarm trials (i.e., error trials in the no-go condition), which resulted in 17 subjects in each group. The 17 students in the high-altitude group (mean age 21.75 ± 1.10 yr; 8 men) were from Tibet University and had lived at high altitude (12,001 ft/3658 m) for 3 yr, whereas the 17 students in the low-altitude group (mean age 21.78 ± 0.85 yr; nine men) had never been to high altitude. There was no significant difference between the two groups in their scores on the national examinations for college entrance ($P > 0.05$), minimizing the likelihood that any group differences could be explained by intelligence-related factors.

Procedure

Subjects were tested individually in a dimly lit room. Visual stimuli were presented against a black background on a computer screen (17″ LCD monitor), with horizontal and vertical visual angles of approximately 5°. Stimuli for the go/no-go task were the capital letters "O" and "X" colored in white. One of the two letters was presented in a single trial and either a response (go) or the withholding of a response (no-go) was required. Each trial began with a go or a no-go stimulus lasting for 150 ms, followed by a black screen. The interstimulus interval range was 1200-1500 ms.

After a practice block of 20 trials, 2 experimental blocks were completed, each consisting of 240 trials with 192 go (80%) and 48 no-go (20%) trials per block. The association between letters and trial type was counterbalanced between the two blocks, with "O" serving as the go stimulus in one block, and as no-go stimulus in the other block. The stimuli were presented and behavioral data were collected using the E-prime software system (Version 1.1, Psychology Software Tools, Inc., Pittsburgh, PA). Stimulus types were presented in a random fashion. Subjects were instructed to press "M" with the right hand on a computer keyboard when a go stimulus occurred and not to respond to no-go stimuli. Speed and accuracy were equally emphasized.

Electroencephalography (EEG) data were recorded from 64 scalp sites (10/20 system) using Ag/AgCl electrodes mounted in an elastic cap (Neuroscan Inc., Charlotte, NC). Electrodes were in-line referenced to a reference site in the middle of the Cz and CPz locations, and off-line rereferenced to the average of the left and right mastoid. Electrode impedances were kept below 5 kΩ. Vertical and horizontal electrooculograms were recorded from above and below the left eye and from the outer canthi of both eyes, respectively. EEG and electrooculogram data were continuously recorded at a sampling rate of 500 Hz, applying a bandwidth filter of 0.05-100 Hz.

Ocular artifacts were removed from the EEG signal using a regression procedure implemented in the Neuroscan software.[19] Epochs were baseline corrected from −400 ms to −200 ms, based on previous ERN/Pe research.[9] The epoch of interest spanned 400 ms prior to the response and 1000 ms afterwards. Within this time window the ERP data were digitally filtered (high pass = 0.05 Hz, low pass = 30 Hz, 24 dB/octave roll off). Artifact rejection was performed to discard epochs contaminated by eye blinks, body movements, and muscle activity. The rejection criterion was a negative or positive change of more

than 75 μV. Averaged waveforms for each individual subject within each condition were calculated.

Statistical Analysis

Data were analyzed using SPSS (SPSS, Inc., Chicago, IL) for Windows. The reaction time for the correct trials, the rate of omission errors in go trials, and the rate of false alarms or commission errors in no-go trials were analyzed. For these behavioral data we employed *t*-tests with group as the independent variable.

We elected to measure ERN at the FCz site, and CRN and Pe at the Cz site. The peak amplitude and latency of the ERN were measured between 0 and 100 ms after a false alarm response, and the mean amplitude of the CRN was measured between 0 and 100 ms after a correct response. The mean amplitude of the Pe component was measured between 150 and 300 ms after a false alarm response. Independent group *t*-tests (two-tailed) were conducted between the high-altitude and low-altitude groups. For all analyses, a 0.05 level of significance was used.

RESULTS

The average omission error rates for the high-altitude and low-altitude group were 1.67 ± 4.05% (mean ± SD) and 0.65 ± 0.80%, respectively; commission error rates were 20.35 ± 11.87% and 19.30 ± 9.41%. The correct response time was 281.48 ± 30.32 ms for the high-altitude group, and 296.04 ± 29.16 ms for the low-altitude group. No significant difference was found in behavioral performance between these two groups ($Ps > 0.05$) (**Fig. 1**).

Fig. 2 depicts response-locked, grand averaged waveforms for correct hit responses of the go condition and false alarm responses for the no-go condition for the high-altitude and low-altitude groups. For the ERN, the high-altitude group had a significantly more negative amplitude compared with the low-altitude group [$t(32) = -2.30$, $P = 0.027$], but no significant difference was found in ERN latency between groups. For the CRN, the high-altitude group also had a significantly more negative amplitude compared with the low-altitude group [$t(32) = -4.11$, $P = 0.0001$]. For Pe, however, there were no significant group differences in the mean amplitude [$t(32) = -0.46$, $P > 0.05$].

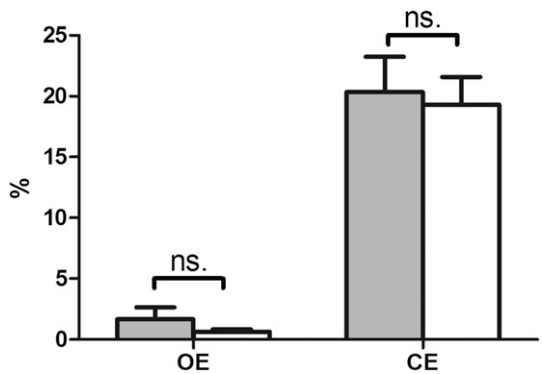

Fig. 1. The average omission error (OE) and commission error (CE) rates for the high-altitude (HA; grey bars) and low-altitude (LA; white bars) groups.

DISCUSSION

In the present study the influence of chronic exposure to high altitude on performance monitoring was investigated using a go/no-go task. Behavioral results did not reveal significant differences between high-altitude and low-altitude groups for either error rates or reaction times. The high-altitude group not only had larger ERN amplitudes following errors, but also had larger CRN amplitudes following correct responses. However, group differences were not found for the Pe component.

Larger ERN amplitudes were found in the high-altitude group than the low-altitude group. The ERN reflects the automatic detection of errors or a mismatch between the actual response and the required response.[4] The enhanced ERN amplitudes in the high-altitude group could be explained as hyperactive error signals due to dysfunction in a comparator mechanism that detects a mismatch between intended and actual responses, reflecting increased sensitivity of error detection.[2] The ERN is generated specifically by the ACC[14]; the results of the present study were consistent with emerging evidence that activation of the ACC may be impaired in high-altitude groups.[28] Similar to our findings in the high-altitude group, previous studies have shown that mental disorders or psychological characteristics are associated with altered performance monitoring. For example, increased ERN amplitude has been observed in obsessive-compulsive disorder,[3] major depressive disorder,[11] and high trait anxiety.[7] These findings on patient groups suggest that pronounced ERN amplitude might be related to cognitive impairment.[2]

As well as the enhanced ERN amplitudes in the high-altitude group, the present study also found enhanced CRN amplitudes, which suggests that performance monitoring is not only altered during error processing, but also during correct response processing. According to previous studies, the enhanced CRN amplitude in high-altitude groups may suggest increased response uncertainty.[15,18] However, uncertainty would enhance the CRN but attenuate ERN amplitudes.[15,18] Enhanced ERN amplitude was found in our study, so the increased CRN amplitudes cannot be explained as reflecting higher uncertainty regarding the correctness of responses. Alternatively, according to a previous study, the ERN and CRN may reflect the combined activity of two underlying processes reflecting differential aspects of performance monitoring: an error-sensitive and an outcome-independent aspect.[1] Therefore, the enhanced CRN and ERN amplitudes in the high-altitude group could be explained as an overactive response checking process or excessive response monitoring that contributes to both components.[8] Several studies have reported pronounced CRN amplitudes in clinical populations, including obsessive-compulsive disorder patients,[3] schizophrenia patients,[12] patients with focal lesions of the lateral frontal

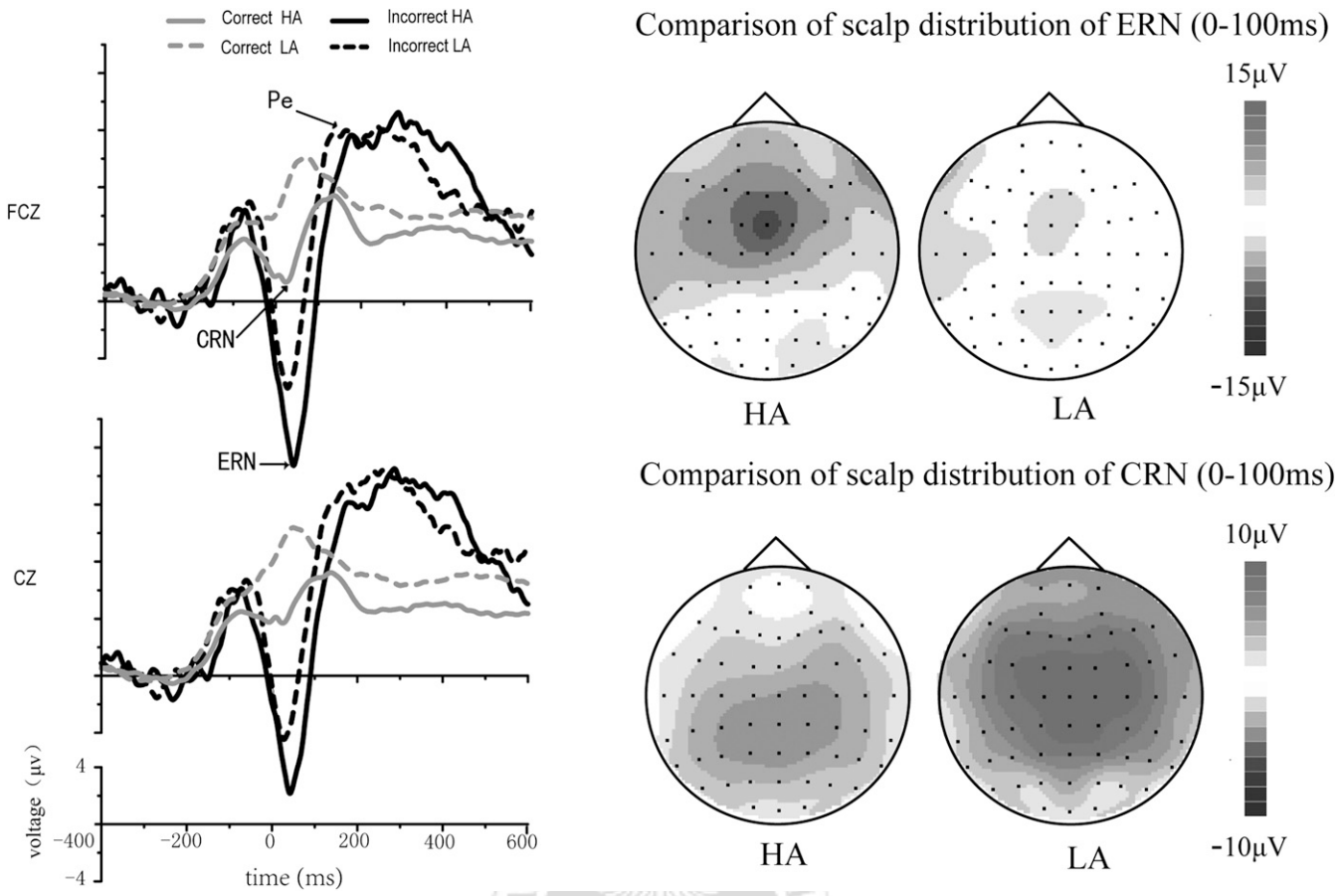

Fig. 2. Left: ERPs time locked to error responses (black lines) and correct responses (grey lines) at FCz and Cz for the high-altitude (HA) and low-altitude (LA) groups. Right: Comparison of the scalp distribution of the ERN and CRN components between the high-altitude and low-altitude groups. The ERN was distributed around the frontocentral scalp area. The group difference in the ERN was expressed more clearly on the topographic map because a higher level of neural activity was found in the high-altitude group compared with the low-altitude group.

cortex,[5] and with left ACC lesions.[22] These findings in patient groups suggest that the pronounced CRN amplitude might be related to cognitive impairment and more specifically to alterations in the performance monitoring system.[2]

High-altitude and low-altitude groups did not differ in their Pe amplitudes. The Pe amplitude reflects an awareness of error commission or deficits.[13] The absence of group differences in the Pe component indicates that this later aspect of performance monitoring is not impaired by long-term high altitude exposure; more specifically, both groups were equally aware of mistakes in performance monitoring.

The disappearance of a group effect in the behavioral results may have been a result of the following reasons. First, it may have occurred because of adaptation that was supported by a compensatory mechanism, which was also found in our previous study.[25] Because the amplitudes of ERP components reflect the levels of neural activity, the increased ERN and CRN amplitudes in the high-altitude group suggested that the high-altitude group engaged a higher level of neural activity to finish the same task compared with the low-altitude group. Moreover, the changes in the levels of neural activity may have influenced the behavioral processing. Second, these results may have been due to the lower sensitivity of the behavioral measure. Because the ERP technique is more sensitive than the behavioral measure, the group difference was obvious in the ERP components. Third, the task that we used may have been too easy for the subjects. Thus, a more difficult task may have resulted in more obvious behavioral effects.

There are two limitations of this research. First, although 3 yr is enough time for complete physical adaptation to 11,811 ft (3600 m),[29] there may still be climatic or cultural effects; thus, physical signs (e.g., ventilation rate, heart rate, blood pH) could be included in future studies. Second, all the subjects in our study were college students, so generalizing of our results should be carried out with caution.

In conclusion, the present study revealed that high altitude effects on performance monitoring included larger ERN and CRN amplitudes in a high-altitude group than in a low-altitude group, suggesting dysfunction in a comparator mechanism and an overactive response checking process or excessive response monitoring. However, the awareness of errors of commission was not changed by long-term exposure to high altitude, as indicated by the unchanging Pe component between the high-altitude and low-altitude groups.

ACKNOWLEDGMENTS

This research was supported by the National Natural Science Foundation of China (Y2JJ081004) and the Key Laboratory of Mental Health, Institute of Psychology, Chinese Academy of Sciences.

Authors and affiliations: Hailin Ma, M.S., B.S., Yan Wang, B.S., Ph.D., Jianhui Wu, B.S., Ph.D., and Buxin Han, Ph.D., M.D., Key Laboratory of Mental Health, Institute of Psychology, Chinese Academy of Sciences, Beijing, China; and Hailan Liu, B.S., M.S., and Ping Luo, B.S., Institute of Education and Psychology, Tibet University, Tibet, China.

REFERENCES

1. Endrass T, Klawohn J, Gruetzmann R, Ischebeck M, Kathmann N. Response-related negativities following correct and incorrect responses: evidence from a temporospatial principal component analysis. Psychophysiology. 2012; 49(6):733–743.
2. Endrass T, Klawohn J, Schuster F, Kathmann N. Overactive performance monitoring in obsessive-compulsive disorder: ERP evidence from correct and erroneous reactions. Neuropsychologia. 2008; 46(7):1877–1887.
3. Endrass T, Schuermann B, Kaufmann C, Spielberg R, Kniesche R, Kathmann N. Performance monitoring and error significance in patients with obsessive-compulsive disorder. Biol Psychol. 2010; 84(2):257–263.
4. Falkenstein M, Hoormann J, Christ S, Hohnsbein J. ERP components on reaction errors and their functional significance: a tutorial. Biol Psychol. 2000; 51(2-3):87–107.
5. Gehring WJ, Himle J, Nisenson LG. Action-monitoring dysfunction in obsessive-compulsive disorder. Psychol Sci. 2000; 11(1):1–6.
6. Gehring WJ, Knight RT. Prefrontal-cingulate interactions in action monitoring. Nat Neurosci. 2000; 3(5):516–520.
7. Hajcak G, McDonald N, Simons RF. Anxiety and error-related brain activity. Biol Psychol. 2003; 64(1-2):77–90.
8. Hajcak G, Simons RF. Error-related brain activity in obsessive-compulsive undergraduates. Psychiatry Res. 2002; 110(1):63–72.
9. Hirsh JB, Inzlicht M. Error-related negativity predicts academic performance. Psychophysiology. 2010; 47(1):192–196.
10. Hochachka PW, Clark CM, Brown WD, Stanley C, Stone CK, et al. The brain at high altitude: hypometabolism as a defense against chronic hypoxia? J Cereb Blood Flow Metab. 1994; 14(4):671–679.
11. Holmes AJ, Pizzagalli DA. Spatiotemporal dynamics of error processing dysfunctions in major depressive disorder. Arch Gen Psychiatry. 2008; 65(2):179–188.
12. Mathalon DH, Fedor M, Faustman WO, Gray M, Askari N, Ford JM. Response-monitoring dysfunction in schizophrenia: an event-related brain potential study. J Abnorm Psychol. 2002; 111(1):22–41.
13. Nieuwenhuis S, Ridderinkhof KR, Blom J, Band GP, Kok A. Error-related brain potentials are differentially related to awareness of response errors: evidence from an antisaccade task. Psychophysiology. 2001; 38(5): 752–760.
14. O'Connell RG, Dockree PM, Bellgrove MA, Kelly SP, Hester R, et al. The role of cingulate cortex in the detection of errors with and without awareness: a high-density electrical mapping study. Eur J Neurosci. 2007; 25(8):2571–2579.
15. Pailing PE, Segalowitz SJ. The effects of uncertainty in error monitoring on associated ERPs. Brain Cogn. 2004; 56(2):215–233.
16. Richardson C, Hogan AM, Bucks RS, Baya A, Virues-Ortega J, et al. Neurophysiological evidence for cognitive and brain functional adaptation in adolescents living at high altitude. Clin Neurophysiol. 2011; 122(9):1726–1734.
17. Ridderinkhof KR, Ullsperger M, Crone EA, Nieuwenhuis S. The role of the medial frontal cortex in cognitive control. Science. 2004; 306(5695): 443–447.
18. Scheffers MK, Coles MG. Performance monitoring in a confusing world: error-related brain activity, judgments of response accuracy, and types of errors. J Exp Psychol Hum Percept Perform. 2000; 26(1): 141–151.
19. Semlitsch HV, Anderer P, Schuster P, Presslich O. A solution for reliable and valid reduction of ocular artifacts, applied to the P300 ERP. Psychophysiology. 1986; 23(6):695–703.
20. Sharma VK, Das SK, Dhar P, Hota KB, Mahapatra BB, et al. Domain specific changes in cognition at high altitude and its correlation with hyperhomocysteinemia. PLoS One. 2014; 9(7):e101448.
21. South M, Larson MJ, Krauskopf E, Clawson A. Error processing in high-functioning autism spectrum disorders. Biol Psychol. 2010; 85(2): 242–251.
22. Swick D, Turken U. Dissociation between conflict detection and error monitoring in the human anterior cingulate cortex. Proc Natl Acad Sci USA. 2002; 99(25):16354–16359.
23. Vidal F, Hasbroucq T, Grapperon J, Bonnet M. Is the 'error negativity' specific to errors? Biol Psychol. 2000; 51(2-3):109–28.
24. Virués-Ortega J, Garrido E, Javierre C, Kloezeman KC. Human behaviour and development under high-altitude conditions. Dev Sci. 2006; 9(4):400–410.
25. Wang Y, Ma H, Fu S, Guo S, Yang X, et al. Long-term exposure to high altitude affects voluntary spatial attention at early and late processing stages. Sci Rep. 2014; 4:4443.
26. Wu J, Yuan Y, Duan H, Qin S, Buchanan TW, et al. Long-term academic stress increases the late component of error processing: An ERP study. Biol Psychol. 2014; 99:77–82.
27. Wu T, Kayser B. High altitude adaptation in Tibetans. High Alt Med Biol. 2006; 7(3):193–208.
28. Yan X, Zhang J, Shi J, Gong Q, Weng X. Cerebral and functional adaptation with chronic hypoxia exposure: a multi-modal MRI study. Brain Res. 2010; 1348:21–29.
29. Zubieta-Calleja G. Human adaptation to high altitude and to sea level: acid-base equilibrium, ventilation and circulation in chronic hypoxia. Saarbrücken (Germany): VDM Publishing; 2010:38–47.