ISSN 2618-1584 Vol. 4, Issue 12: 41-45, DOI: 10.25236/FMSR.2022.041207

Effect of the Oxygen Intervention on Cognitive Function at High Altitude and Mechanism of Action

Yuming Zhang[1], Chenxiao Han[1,*]

[1]School of Education, Tibet University, Lhasa, Tibet, 850001, China
**Corresponding author*

Abstract: *Previous studies on oxygen intervention in high altitude environment mainly emphasize on the improvement effect of oxygen intervention on acute and chronic plateau diseases and various diseases, but there are fewer studies on the improvement of cognitive function of wholesome plateau people by oxygen intervention. This paper will further review the effect of oxygen intervention on cognitive function at high altitude from the application of oxygen intervention in high altitude environment, and explore its inner mechanism, which will provide new aspects for future research and have practical guidance significance for healthy life of plateau people.*

Keywords: *high altitude, oxygenation, cognitive function*

1. Introduction

When people are exposed to low-pressure and low-oxygen environments at altitude, a series of physiological and pathological changes will occur, such as arterial hypoxia[1], chronic altitude sickness[2], and altitude decline[3].Clinically, oxygen inhalation is divided into hyperbaric oxygen and normobaric oxygen according to pressure and oxygen concentration. Normobaric oxygen has excellent curative effect, and high-pressure oxygen has strong penetration, so that tissue cells that cannot be reached by oxygen under general normobaric pressure can also obtain sufficient oxygen supply. On this basis, the potential opportunities, limitations, ethical issues of oxygen therapy for neural reinforcement and the neurocognitive reinforcement of healthy adults have also been widely discussed in society[4,5,6]. This paper will clarify the effects of high altitude environment on individuals and select appropriate programs to intervene.

2. Oxygen Intervention in High Altitude Environments

After entering the hypoxic environment at high altitude, the human body appears as the lung to adapt to the hypoxic environment increased arterial pressure, increased red blood cells and increased hemoglobin are beneficial to oxygen exchange and transportation, called plateau acclimatization. Brain is the most active organ in human metabolism. Although adult brain does not grow, divide or move, it consumes up to 25% of blood oxygen supply[7]. Therefore, oxygen is very important for mental activities of the brain. Oxygen supply is also considered as a neurocognitive enhancer, which is widely used in various brain diseases and healthy subjects. In recent years, with the development of cognitive neuroscience and technology, some functional magnetic resonance imaging (fMRI) studies have also reported the neural mechanism of oxygen induced cognitive enhancement, which provides a certain physiological basis. High altitude environments is characterized by low pressure, low oxygen, dryness & strong ultraviolet rays, etc. People who come to high altitude will sustain plateau reactions, and rehabilitation treatments such as hyperbaric oxygen are used clinically to improve individual hypoxia reactions. In the anoxic environment at high altitude, it can effectively improve the human anoxic symptoms by supplying high concentration oxygen enriched gas to the personnel. At present, the methods of oxygen inhalation mainly include nasal tube method (nasal suction tube), nasal obstruction method, mask method, mask method, head mask method and oxygen tent method [1]. Among them, nasal tube oxygen inhalation refers to inserting the nasal oxygen tube into the user's nasopharynx for oxygen inhalation. This oxygen inhalation method is simple to operate and easy to use, and is widely used in the field of home oxygen therapy and oxygen supply in plateau areas. Oxygen intervention also has better effect in improving high altitude sleep disorder[8], postoperative oxygen saturation of patients[9], respiratory failure[10], plateau disease[11], and hypertension[12]. On this basis, we will continue

ISSN 2618-1584 Vol. 4, Issue 12: 41-45, DOI: 10.25236/FMSR.2022.041207

to explore the effect of oxygen intervention on cognitive function from the clinical and cognitive aspects.

It is common for oxygen intervention to improve various symptoms in plateau areas, but at present, oxygen supply resources are precious. High flow and long-term inhalation of oxygen not only increase the cost, but also may cause oxygen poisoning and excessive dependence on oxygen. In the plateau environment, how to determine the optimal oxygen supply flow and time and carry out scientific oxygen supply is of great significance for the prevention of plateau diseases. Therefore, we will further explore the best oxygen absorption scheme that can effectively improve the hypoxia of the body.

3. Effect of oxygen intervention on cognitive function at high altitude

Cognitive function refers to the brain's ability to process, store, and extract information, including multiple aspects of learning, memory, perception, attention, language, thinking, and logical reasoning[13]. Human tissues, especially neural tissues, are the most sensitive to changes in the internal and external environment. Under hypoxia conditions, damage to brain functions (especially higher brain functions such as learning, memory, thinking and emotional-emotional functions) occurs earliest and is more severe, and the longer the exposure, the more severe the damage[14].

Hyperbaric oxygen therapy (HBO) is a method of breathing pure oxygen or high concentration oxygen under high pressure (above normobaric pressure) to treat hypoxia diseases and related diseases. The physiological basis of HBO treatment of diseases is mainly to improve blood oxygen tension and increase blood oxygen content; Improve the diffusion rate of blood oxygen and increase the effective diffusion distance of oxygen in the tissue[15]. It can improve cognitive impairment caused by some diseases by increasing tissue oxygen. Cognitive function refers to the brain's ability to process, store and extract information, including learning, memory, perception, attention, language, thinking and logical reasoning[16]. Cognitive impairment will lead to a certain degree of cognitive dysfunction. Hyperbaric oxygen therapy combined with basic drug therapy has a better effect on all kinds of cognitive dysfunction.

From the cases of clinical treatment, we confirm that manipulating the level of oxygen does have an impact on cognition. In psychological research, few people have studied the possibility of cognitive enhancement of healthy adults after the increase of oxygen concentration. Some evidence shows that the management of oxygen concentration and pressure can improve cognitive level. We will elaborate its effects on memory, attention and sensory perception under hyperbaric oxygen intervention. Ma et al[17]found that long-term high altitude exposure affected the retention of visual working memory and the spatial memory ability of transplants as well as the level of attention orientation of secular residents. Ma also found that prolonged high altitude exposure impaired the retention of visual working memory and spatial memory ability of migrants as well as the level of attention orientation and over-activation of their executive control levels; in terms of attention, prolonged high altitude exposure impaired the level of alertness, orientation and executive control of migrants[18]; prolonged high altitude exposure increases the response time of conversion functions, but is inconclusive in executive functions[19].

Normobaric oxygen (NBO) often refers to high flow oxygen inhalation therapy outside the cabin, which refers to an oxygen inhalation method in which patients breathe high concentration oxygen with a mask to treat diseases at a standard normobaric pressure of 25 ℃. NBO can increase the physical dissolved oxygen in the blood, increase the arterial oxygen partial pressure of the aorta, and play a neuroprotective role in rapidly penetrating the blood-brain barrier. NBO is superior to other drugs and other treatment methods, and plays a unique role in clinical practice[20]. In psychological research, the effects of intervention with different oxygen concentrations under normobaric pressure on cognitive function of different individuals are different, and it is easier to operate oxygen concentration variables, which verifies the different effects of NBO and HBO[21]. NBO is effective in the early and long-term treatment of cognitive dysfunction caused by stroke, but its exact treatment time window and treatment cycle still need to be carefully designed and confirmed by multi center, large sample randomized controlled studies. In the case of normobaric hypoxia, Li Guoqing et al[22] found that intermittent normobaric hypoxia treatment will aggravate cognitive dysfunction in the early stage, and is an effective measure to treat cognitive dysfunction caused by chronic cerebral blood flow hypoperfusion caused by disease in the late stage. The research perspective of normobaric hypoxia included in the time and treatment period needs to be broader and long-term. Five years later, their further study verified that repeated normobaric hypoxia can improve white matter injury and cognitive dysfunction in rats with chronic cerebral ischemia, but its research object is limited to animals, and the test capacity

ISSN 2618-1584 Vol. 4, Issue 12: 41-45, DOI: 10.25236/FMSR.2022.041207

can be further expanded in the future.

The current study found that the use of oxygen intervention improves cognitive function. At high altitude hypoxia, individuals produce a significant decrease in attention, whereas with hyperbaric oxygen intervention, subjects' attention transfer ability and attention breadth are increased[23]. The oxygen intervention may improve hypoxia and further improve cognitive function by improving the individual's blood oxygen saturation, but the underlying mechanism is inconclusive.

4. Summary

In terms of micro physiological mechanism, in the direction of vascular promotion, although some studies have found that oxygen inhalation can improve cognitive function by promoting cerebral angiogenesis, the view that adequate blood supply can promote brain plasticity by providing rich nutrition is still in the stage of theoretical speculation. More research is needed in the future to investigate the role of nutrition supply and neurotransmitter synthesis in brain angiogenesis and brain plasticity. In addition, in the direction of disease intervention, it is also proved that the degree of damage to brain structure caused by disease will vary according to the different ways of oxygen inhalation, but the regulatory role of oxygen inhalation between disease and brain biochemical reaction is still unclear[24]. How different oxygen inhalation methods regulate the energy metabolism process of patients' brain and ultimately affect brain structure and brain function needs to be further explored in the future. Secondly, the existing research results need to be further integrated. For example, although studies have found that BDNF induced by oxygen therapy can promote central executive function and memory[25], Chen et al have found that BDNF induced by oxygen therapy cannot affect central cognitive function[26] Inconsistent research results may be caused by different oxygen inhalation duration and oxygen concentration, or by different subjects and cognitive ability measurement methods. Further integration is needed in the future.

There are not many studies on the effect of oxygen intervention on cognitive function, and the main reality is in memory and attention. There are not many previous studies on the effect of oxygen intervention on healthy humans, Chung et al[27] found that healthy individuals who inhaled oxygen before learning had improved memory levels, while inhaling compressed air did not have the same effect. Next, we can further explore in other aspects of oxygen intervention to improve cognitive function such as executive control, and secondly, we can study the dose effect of oxygen intervention to develop a suitable high altitude oxygen regimen for healthy individuals.

There are also some deficiencies in the study of macro mechanism. Although the study found that oxygen inhalation may promote cerebral angiogenesis by increasing the activation level of frontal lobe and other brain regions[28], no research has focused on why it is in different brain regions. In the future, it is necessary to further explore this problem by integrating factors such as cerebral angiogenesis, synaptic connection generation and neuronal energy consumption. Secondly, the effects of different ways of oxygen inhalation therapy on brain structure and brain function are still unclear. In the future, we should combine morphological anatomy and non-invasive brain imaging technology to investigate the effects of oxygen inhalation frequency, duration and oxygen concentration on the brain, and improve its interpretation mechanism. In terms of research content, the combined treatment of oxygen therapy and other therapies is currently mainly combined with aerobic training and cognitive ability improvement training. There is an analysis of the effect of oxygen therapy combined with drug therapy and aerobic training. Different drug treatments such as anesthetics have an impact on the effect of oxygen therapy, and it is unknown whether other drug treatments will also affect the effect of oxygen therapy[29]; However, there are a lot of studies on aerobic training in the treatment of cognitive impairment caused by brain injury, and the effect of combined treatment is better than that of simple oxygen therapy. In the future, we can add aerobic exercise training to oxygen therapy, and select healthy people in hypoxic environment as subjects to observe whether impaired cognition can be improved[30-31].

Acknowledgments

This work was supported by the “High-level Talents Training Program ” for postgraduates of Tibet University, Project (Project No. 2020-GSP-S154).

ISSN 2618-1584 Vol. 4, Issue 12: 41-45, DOI: 10.25236/FMSR.2022.041207

Declaration of Competing Interest

The authors have no conflicts of interest to declare that are relevant to the content of this article.

References

[1] Yang S.Y., Feng E.Z., Yan Z.Q., Zhang E., He W., & Tian Z.X., et al. (2012). Hypoxia and Tumor Necrosis Factor System Activity in Chronic Obstructive Pulmonary Disease Combined with Chronic Pulmonary Heart Disease in Highlands and the Impact on Malnutrition. Chinese Journal of Lung Diseases (electronic version) (03), 17-21.
[2] Wu, T.I.. (2012). Recent advances in the study of chronic plateau diseases on the Tibetan Plateau in China. Chinese Journal of Practical Internal Medicine, 32(5), 3.
[3] Wang, Yaping, & Geri. (2012). Advances in the study of altitude decline disorder. Chinese Medical Journal, 92(32), 3.
[4] Partridge B J, Bell S K, Lucke J C, et al. Smart Drugs "As Common As Coffee": Media Hype about Neuroenhancement[J]. Plos One, 2011, 6(11):e28416.
[5] Graf W D, Nagel S K, Epstein L G, et al. Pediatric neuroenhancement: ethical, legal, social, and neurodevelopmental implications[J]. Neurology, 2013, 80(13):1251-1260.
[6] Heinz A, Kipke R, S Müller, et al. True and false concerns about neuroenhancement: a response to 'Neuroenhancers, addiction and research ethics', by D M Shaw[J]. Journal of Medical Ethics, 2014, 40(4).
[7] Roland P E, Levin B, Kawashima R, et al. Three-dimensional analysis of clustered voxels in 15 O-butanol brain activation images[J]. Human Brain Mapping, 1993, 1(1):3–19.
[8] Ha ZD, Zhu JY, & Jane XL. (2015). Effects of different interventions on sleep sao2 in youth migrating to 5380m above sea level. Journal of Highland Medicine (4), 5.
[9] Xie S. W., Li W. J., Zhao H., & Wang T. H.. (2019). Effect of different oxygenation flow rates on postoperative oxygen saturation in patients at high altitude plateau. Surgical Theory and Practice (2), 4.
[10] Wang, Zhen. (2008). Oxygen therapy for patients with respiratory failure in pulmonary heart disease at high altitude. Chinese and Foreign Medical Science (16), 1.
[11] Duan, Jinqing, Liu, Zheng, & Liu, Hongbin. (2007). Comparison of the efficacy of hyperbaric oxygen and normobaric mask oxygenation in the treatment of acute mild plateau sickness. Chinese Journal of Marine Medicine and Hyperbaric Medicine, 14(3), 2.
[12] Chen, J., Zheng, B. H., Yan, Y. P., Li, S. H., Zheng, J. P., & Guo, J. et al. (2014). Effect of oxygen therapy on correlation of blood pressure changes in plateau at different altitudes. Proceedings of the 10th National Conference on Integrative Medicine and Disaster Medicine in Jiangsu Province, 2014.
[13] Barkley RA, Edwards G, Laneri M, Fletcher K, Metevia L (2001) cognitive functioning, temporal discounting, and sense of time in adolescents with attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD). J A born Child Psychology 29:541–556.
[14] Yang GY, Feng ZZ, Wang T. Effects of altitude hypoxia on psychological function and protection [J]. Chinese Behavioral Medicine Science, 2003, 12(004): 471-3.
[15] Wang Hongyun, Cui Jianhua, Jin Xianghua. Research Progress on anti hypoxia effect of hyperbaric oxygen and prevention and treatment of altitude sickness [J]. Journal of high altitude medicine, 2009 (01): 58-61.
[16] Li Zhijing, Jin Xianglan. Research progress of oxygen therapy for acute ischemic stroke [J]. Medical review, 2020, v.26 (02): 104-108.
[17] Ma H-L, Zhang X-J, Yang Z-T. Effects of long-term high-altitude exposure on attention networks of migrants and sedentary residents [J]. Chinese Journal of Plateau Medicine and Biology, 2017, 38(004): P.267-72.
[18] Wang, Y., Ye, A., Peng, D., Miao, C., Di, Z., & Gong, W. (2022). Spatiotemporal variations in water conservation function of the Tibetan Plateau under climate change based on INVEST model. Journal of Hydrology: Regional Studies, 41, 101064.
[19] Glass, J. M., Buu, A., Adams, K. M., Nigg, J. T., & Zucker, R. A. (2010). Effects of alcoholism severity and smoking on cognitive neurocognitive function. Addiction, 104(1), 38-48.
[20] Peng Huiping, Lu Xiaoxin, Tang Yongjian, et al. Clinical application of atmospheric oxygen therapy [J]. Journal of Fuzhou General Hospital, 2005, 34 (003): 651-652.
[21] Lu Xiaoxin, Tang Yongjian, He Suyu. Effect of combined therapy of normobaric oxygen and hyperbaric oxygen on severe brain injury [J]. Chinese clinical rehabilitation, 2002.
[22] Li Guoqing, Meng ran, Ren Changhong, et al. Effects of intermittent normobaric hypoxia post adaptation on cerebral white matter injury and cognitive dysfunction in rats with chronic cerebral

ISSN 2618-1584 Vol. 4, Issue 12: 41-45, DOI: 10.25236/FMSR.2022.041207

blood flow hypoperfusion [J]. Chinese Journal of geriatric cardiovascular and cerebrovascular diseases, 2013, 005 (005): 530-535.
[23] Bu, Xiao-Ou, Yang, Xiyue, Zhang, Delong, & Ma, Hailin. 2011 A new species of the genus Phyllostachys (Hymenoptera, Braconidae) from China. (2021). Single hyperbaric oxygen intervention improves attentional network in high-altitude transplants. Journal of Physiology.
[24] Yu Ning, Li Tong, Huang Qiliang, et al. Clinical study on the effect of early hyperbaric oxygen therapy on cerebral blood perfusion and prognosis in patients with acute cerebral infarction [J]. Stroke and neurological disease, 2013 (01): 43-45.
[25] Leckie R L, Oberlin L E, Voss M W, et al. BDNF mediates improvements in executive function following a 1-year exercise intervention[J]. Frontiers in Human Neuroscience, 2014, 8(985):985.
[26] Chen, F C, Wang, et al. Impact of acute aerobic exercise and cardiorespiratory fitness on visuospatial attention performance and serum BDNF levels[J]. Psychoneuroendocrinology: An International Journal, 2014, 41:121-131.
[27] Chung S C, Tack G R, Choi M H, et al. Changes in reaction time when using oxygen inhalation during simple visual matching tasks[J]. Neuroscience Letters, 2009, 453(3):175-177.
[28] Qin Jie, you Chunjing. Effect of hyperbaric oxygen on the number of choline acetyltransferase positive neurons in frontal cortex and hippocampus of rats with brain injury [J]. Chinese Journal of physical medicine and rehabilitation, 2006, 28 (5): 302-304.
[29] Leckie R L, Oberlin L E, Voss M W, et al. BDNF mediates improvements in executive function following a 1-year exercise intervention[J]. Frontiers in Human Neuroscience, 2014, 8(985):985.
[30] Gu binliang, Roger Effect of hyperbaric oxygen chamber combined with aerobic training on cognitive function of patients with moderate brain injury [J]. Chinese Journal of practical neurological diseases, 2017, 20 (023): 43-45.
[31] Tian Feng, Hu Lixun. Effects of aerobic exercise combined with hyperbaric oxygen on cognitive function, blood-brain barrier and oxygen free radicals in rats with global cerebral ischemia-reperfusion [J]. Chinese Journal of Nautical Medicine and high pressure medicine, 2018, 025 (002): 81-85.